U.S. Army Center for Health Promotion and Preventive Medicine

USCHPPM

TOXICOLOGY STUDY NO. 85- XC-5131-03
PROTOCOL NO. 5131-38-02-12-01
SUBCHRONIC ORAL TOXICITY OF
RDX IN RATS
JANUARY 2006

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Readiness Thru Health

U.S. Army Center for Health Promotion and Preventive Medicine

The lineage of the U.S. Army Center for Health Promotion and Preventive Medicine (USACHPPM) can be traced back over 50 years. This organization began as the U.S. Army Industrial Hygiene Laboratory, established during the industrial buildup for World War II, under the direct supervision of the Army Surgeon General. Its original location was at the Johns Hopkins School of Hygiene and Public Health. Its mission was to conduct occupational health surveys and investigations within the Department of Defense's (DOD's) industrial production base. It was staffed with three personnel and had a limited annual operating budget of three thousand dollars.

Most recently, it became internationally known as the U.S. Army Environmental Hygiene Agency (AEHA). Its mission expanded to support worldwide preventive medicine programs of the Army, DOD, and other Federal agencies as directed by the Army Medical Command or the Office of The Surgeon General, through consultations, support services, investigations, on-site visits, and training.

On 1 August 1994, AEHA was redesignated the U.S. Army Center for Health Promotion and Preventive Medicine with a provisional status and a commanding general officer. On 1 October 1995, the nonprovisional status was approved with a mission of providing preventive medicine and health promotion leadership, direction, and services for America's Army.

The organization's quest has always been one of excellence and the provision of quality service. Today, its goal is to be an established world-class center of excellence for achieving and maintaining a fit, healthy, and ready force. To achieve that end, the CHPPM holds firmly to its values which are steeped in rich military heritage:

- ★ *Integrity is the foundation*
- ★ *Excellence is the standard*
- ★ *Customer satisfaction is the focus*
- ★ *Its people are the most valued resource*
- ★ *Continuous quality improvement is the pathway*

This organization stands on the threshold of even greater challenges and responsibilities. It has been reorganized and reengineered to support the Army of the future. The CHPPM now has three direct support activities located in Fort Meade, Maryland; Fort McPherson, Georgia; and Fitzsimons Army Medical Center, Aurora, Colorado; to provide responsive regional health promotion and preventive medicine support across the U.S. There are also two CHPPM overseas commands in Landstuhl, Germany and Camp Zama, Japan who contribute to the success of CHPPM's increasing global mission. As CHPPM moves into the 21st Century, new programs relating to fitness, health promotion, wellness, and disease surveillance are being added. As always, CHPPM stands firm in its commitment to Army readiness. It is an organization proud of its fine history, yet equally excited about its challenging future.

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14. ABSTRACT

1,3,5-trinitro-1,3,5-triazine, commonly known as RDX, is a military explosive that has been extensively used by the U.S. Military since the late 1930's and has been reported to cause convulsions in military field personnel and munition workers during use and manufacture. In addition, military bases across the United States have been contaminated due to the testing and disposal of RDX. Thus, human exposure is possible both during remediation processes and through groundwater contamination. This report outlines a progressive series of three oral toxicity studies on RDX that were designed to identify effect levels, define target organs, support regulatory actions, and provide risk assessment information. Male and female Fischer 344 rats were dosed 7 days a week for a period of 13 weeks at dosages of 0, 4, 8, 10, 12, and 15 mg/kg/day. The RDX was suspended in a solution of 1% Methylcellulose/ 0.2% Tween 80 in distilled water. Male and female dose dependent mortality, as well as other measured parameters, was observed at dosages of 8 mg/kg/day and above. The No Observed Adverse Effect Level for this study was 4 mg/kg/day, based on mortality.

15. SUBJECT TERMS

oral toxicity, explosives, subchronic oral exposure, RDX, 1,3,5-trinitro-1,3,5-triazine

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Subchronic Oral Toxicity of RDX in Rats
Toxicology Study No. 85-XC-5131-03
Protocol No. 5131-38-02-12-01

Data Requirement

Health Effects Testing Guidelines Reference No. OPPTS 870.3100

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Study Completed On

30 January 2006

Performing Laboratory

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Laboratory Project ID

Protocol No. 5131-38-02-12-01

STATEMENT OF NO DATA CONFIDENTIALITY CLAIMS

This is a complete and unaltered copy of this report, as received from U.S. Army Center for Health Promotion and Preventive Medicine (USACHPPM), Directorate of Toxicology.

No claim of confidentiality is made for any information contained in this report on the basis of its falling within the scope of TSCA.

Organization: U.S. Army Environmental Center, Range Operations Support Branch

Organization's Agent: Michael J. Dette

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7/31/06
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GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

This study does not meet the requirements of 40 CFR Part 160, and differs in the following ways:

1. The Directorate of Toxicology archiving room is not of adequate size to allow for orderly storage and timely retrieval of studies.

2. The Directorate of Toxicology archiving room does not have a fire suppression system.

Submitted By:

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Applicant/Submitter:

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Date

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MCHB-TS-TTE

EXECUTIVE SUMMARY
TOXICOLOGICAL STUDY NO. 85-XC-5131-03
PROTOCOL NO. 5131-38-02-12-01
SUBCHRONIC ORAL TOXICITY OF RDX IN RATS
SEPTEMBER 2004 – JANUARY 2006

1. PURPOSE. These studies were conducted to determine the subchronic oral toxicity of RDX (1,3,5-trinitro-1,3,5-triazine), a commonly used military explosive, in laboratory rats. This information, along with the results from other laboratory animal toxicity studies, will provide a no observed adverse effect level (NOAEL) to predict the potential risk to human health upon exposure to this compound. This NOAEL value will, in turn, allow for an accurate adjustment to the current Environmental Protection Agency (EPA) established reference dose (RfD). These reference doses are typically used to determine clean-up guidelines at contaminated areas on various military installations.

2. CONCLUSIONS.

a. RDX administered orally 7 days per week for 90 days induced lethality at dosages of 8 mg/kg/day and higher in both male and female rats. Visible signs of toxicity in the 8, 10, 12, and 15 mg/kg/day dose groups included changes in arousal, blepharosis, increased salivation, blood stains around the mouth and nose, rough haircoat, tremors, and convulsions.

b. Measured signs of toxicity included alterations in brain, testes, epididymus, body, spleen, kidney, and liver weights and weight ratios, as well as urine production. Alterations in hematology and clinical chemistry also occurred. Histopathology performed on collected tissues from the control and 15 mg/kg/day dose groups revealed no treatment-related alterations. All visible and measured signs of toxicity were confined to dose groups that also produced lethality.

c. Immunotoxicity studies indicated that no adverse immunological effects occurred as a result of 90-day oral exposure to RDX.

d. The NOAEL for subchronic oral exposure to RDX for 90-days, as determined from this study, is 4 mg/kg/day based on lethality.

CONTENTS

Appendices (cont)

TOXICOLOGICAL STUDY NO. 85-XC-5131-03
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SUBCHRONIC ORAL TOXICITY OF RDX IN RATS
SEPTEMBER 2004 – JANUARY 2006

1. REFERENCES. See Appendix A for a listing of references.

2. AUTHORITY. This study was performed to fill a data need for the U.S. Army Environmental Center (AEC), Range Operations Support Branch, APG-EA, MD 21010-5401.

3. PURPOSE. These studies were conducted to determine the subchronic oral toxicity of RDX (1,3,5-trinitro-1,3,5-triazine), a commonly used military explosive, in laboratory rats. This information, along with the results from other laboratory animal toxicity studies, will provide a no observed adverse effect level (NOAEL) to predict the potential risk to human health upon exposure to this compound. This NOAEL value will, in turn, allow for an accurate adjustment to the current Environmental Protection Agency (EPA) established reference dose (RfD). These reference doses are typically used to determine clean-up guidelines at contaminated areas on various military installations.

4. GENERAL BACKGROUND.

a. RDX, a military explosive, has been extensively used by the U.S. Military since the late 1930's and has been reported to cause convulsions in military field personnel who ingest it and in munition workers inhaling its dust during manufacture. In addition, military bases across the United States have been contaminated due to the testing and disposal of RDX, along with other explosive compounds (reference 1). Due to this contamination, human exposure is possible both during remediation processes and through groundwater contamination.

b. The current reference dose established for RDX was determined using data from a U.S. Army sponsored chronic study performed on rats in 1983 (reference 2). However, the NOAEL for this study was based on inflammation of the prostate gland, which is a common condition in older rodents and generally not due to the toxicity of the compound being administered. Since 85% of the animals exhibiting this condition were found dead or near death, it is likely that they simply had a bacterial infection. In addition, the RDX used in conducting the previous study was military grade RDX containing other explosives and impurities and the rats were given the RDX indirectly by mixing it with their feed. Based on the results of the previous study, the NOAEL was set at 0.3 mg/kg/day and the RfD was set at .003 mg/kg/day after the addition of uncertainty factors. Compliance to these standards at contaminated military sites would appear to be overly conservative and extremely costly. These current studies were designed to provide a much more realistic standard and allow for less expensive remedial efforts at these sites.

c. This document will report the conduct, findings, and conclusions of a progressive series of three oral toxicity studies performed with RDX in laboratory rats. The series consisted of an approximate lethal dose (ALD), a 14-day repeated dose study, and a 90-day subchronic study. Such investigations have been shown to identify effect levels, define target organs, support regulatory actions, and provide risk assessment information.

d. A literature search was conducted prior to the initiation of the range-finding studies. Although previous oral toxicity work has been performed in rats, the RDX was typically administered in the feed rather than via oral gavage and toxicity values varied greatly depending on such factors as the RDX purity, particle size, and signs of toxicity identified. Reported NOAEL values ranged from 0.3 mg/kg/day to 80 mg/kg/day while rat LD50 values ranged from 50 mg/kg to 300 mg/kg. These values were used as a starting point in establishing dosage levels for the ALD described herein, but varied too greatly to preclude the range-finding studies. RDX is reported to cause irritation of the skin, eyes, nose, and throat in addition to kidney damage and a variety of central nervous system effects. There is limited evidence that RDX causes cancer of the liver.

e. This study protocol was initially approved by the U.S. Army Center for Health Promotion and Preventive Medicine (USACHPPM) Institutional Animal Care and Use Committee (IACUC) in December 2002 and initiated in March 2003. Due to unavoidable complications with the RDX/diluent mixing process, the study was aborted in April 2004. A modification was submitted to the original protocol suggesting that the study be repeated and was approved in August 2004. The results of the repeated study will be reported herein. The results of both the aborted study and the reported study will be archived under protocol number 5131-38-02-12-01, but will be individually identified.

f. The following table identifies the critical dates of the 90-day study.

Table 1. Critical dates of 90-day study

Critical Event	**Date of Event**
Protocol (Modification to Repeat) Approved	08/06/04
Animals Received	10/13/04
Study Start	10/26/04
Experimental Start	10/26/04
Experimental Completion	02/09/05
Necropsy Start	01/25/05
Necropsy Completion	02/09/05
Study Completion	01/30/06

5. MATERIALS.

a. Test Substance. Neat RDX (1,3,5-trinitro-1,3,5-triazine) was procured from the Department of the Navy, Naval Ordnance and Security Activity, Farragut Hall Bldg. D-323, 23 Strauss Avenue, Indian Head, MD 20640-5555. The RDX, Lot # 0858500 Batch # 01B-012, was analyzed for purity prior to shipping and found to be 99.99%. The material was then wetted

with no less than 15% water by mass and shipped to Joe Domanico, Research, Development, and Engineering Command (RDECOM), Engineering Directorate, Pyrotechnics Team, APG-EA, MD 21010 for storage. Due to the explosive nature of RDX, all neat compound manipulation, including drying, weighing, and initial mixing with the methylcellulose diluent was performed by the Chromatographic Analysis Division (Explosives Team), Directorate of Laboratory Sciences (DLS), USACHPPM. A 90-day stability test was performed by DLS on the RDX/Methylcellulose/Tween 80 suspension with the results indicating that the RDX concentration remained stable throughout the 90-day period. Fresh suspensions were made once a month in order to facilitate mixing and dosing. Each bottle of dosing suspension was mixed using a magnetic stir bar until a uniform suspension was obtained and continued to be mixed each day during the dosing procedure. In addition, each batch of dosing solution was analyzed prior to use with a gas chromatograph (electron capture detector) to verify the RDX concentration.

b. Animals.*† All studies were conducted using young adult male and female Fischer 344 rats obtained at 5 weeks of age from Charles River Laboratories, Wilmington, Massachusetts. The Attending Veterinarian examined the animals and found them to be in acceptable health. The animals were quarantined for 2-4 week periods after their arrival in this facility. All rats were maintained in a temperature-, relative humidity-, and light-controlled room. The conditions were 64-79°F, 30% to 70% relative humidity with a 12-hour light/dark cycle (reference 3). A certified pesticide-free rodent chow (Harlan Teklad®, 8728C Certified Rodent Diet) and drinking quality water were available *ad libitum* (reference 4). Rats were housed individually in suspended polycarbonate boxes with Harlan Sani-Chip® bedding. Ophthalmic examinations were performed prior to the scheduled start of the 90-day study and within 2 weeks of the scheduled necropsies. A total of 4 male and 4 female rats not chosen for these studies, but housed in the same room, were returned to the Charles River Laboratories periodically to assess the general health of the purchased animals. Serology, bacteriology, pathology, and parasitology evaluations were performed. Each rat was uniquely identified by number using cage cards and microchip implants (BioMedic Data Systems, Inc., Maywood, New Jersey).

c. Contract Studies. Dr. George A. Parker, DVM, Hillsborough, North Carolina, performed histopathological evaluations for both the 14-day and 90-day studies under commercial contract DAAD05-94-D-7043. Dr. Ann Schiavetta, DVM, MAJ, VC, Attending Veterinarian, USACHPPM and Dr. Wilfred McCain, PhD, Toxicologist, USACHPPM, performed the in-house review.

d. Quality Assurance. The USACHPPM Quality Systems Office audited critical phases of these studies. Appendix B provides the dates of these audits along with the audited phase.

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* Research was conducted in compliance with DOD and Federal statutes and regulations relating to animals and experiments involving animals and adheres to principles stated in the Guide for the Care and Use of Laboratory Animals, Institute of Laboratory Animal Resources, Commission on Life Sciences, National Research Council. National Academy Press, Washington, D.C. 1996.

† The studies reported herein were performed in animal facilities fully accredited by the American Association for the Accreditation of Laboratory Animal Care.

® Teklad Certified Rat Diet is a registered trademark of Harlan, Teklad, Madison, Wisconsin.

® Harlan Sani-Chip is a registered trademark with P.J. Murphy Forest Products Corporation, Montville, New Jersey.

e. Study Personnel. Appendix C contains the names of persons contributing to the performance of these studies.

6. METHODS.

a. Approximate Lethal Dose.

(1) An ALD was performed in male and female rats in accordance with the Toxicology Directorate Standard Operating Procedure (SOP) for ALD Procedures (reference 5).

(2) A suspension of RDX/Methylcellulose/Tween 80 in distilled water was administered to 8 rats of each sex in single oral graduated doses of 20, 30, 45, 68, 101, 152, 228, or 342 mg/kg. A 16 GA x 2-inch stainless steel gavage needle was used to facilitate oral dosing. One additional rat of each sex served as a Methylcellulose/Tween 80 control group. Four dosing suspensions were mixed to keep the dosing volumes relatively consistent.

(3) Following the administration of the test compound, the rats were observed for 14 days. All clinical signs or incidences of death were recorded on a daily basis. Individual body weights were recorded daily (5 days a week) throughout the 14-day observation period.

(4) Surviving animals were euthanized on day 14 and submitted for gross pathological examination. The lowest dose that caused death (with no animals living at higher doses and no deaths at lower doses) during the 14-day observation period was considered to be the ALD of the test substance.

b. 14-Day Oral Repeated Dose Toxicity Study.

(1) Upon evaluating the results of the ALD, a 14-day range-finding oral toxicity study was conducted in male and female rats in accordance with the Toxicology Directorate SOP for 14-day Range Finding and 90-Day Oral Toxicity Study in Rats (reference 6).

(2) In this phase of the study 48 male and 48 female Sprague-Dawley rats, 5 weeks old, were used. Following a quarantine/acclimatization period, the animals were randomly distributed using the LABCAT® randomization program into eight treatment groups consisting of six male and six female rats each. Dosage levels were set at 0 (negative control), 2.125, 4.25, 8.50, 17.00, 25.50, 34.00, and 42.5 mg/kg/day. A staggered start of approximately one week between males and females was used to facilitate scheduling of necropsies. Negative control animals were dosed with the 1% Methylcellulose/0.2% Tween 80 in distilled water diluent solution at the same volume per body weight as all other dose groups (4 ml/kg).

(3) In an effort to obtain accurate food consumption data, separate suspensions were mixed so that the volume per kilogram of body weight (4 ml/kg) remained the same for each dose group. The RDX suspensions and diluent control were administered daily (7 days per week, total of 14 doses) for the 14-day study. A 16 GA x 2-inch stainless steel gavage needle

®LABCAT is a registered trademark of Innovative Programming Associates, Princeton, New Jersey.

was used to facilitate oral dosing. The suspensions were sampled and analyzed to verify the concentrations and stability prior to the first day of dosing the male rats.

(4) Body weights and feeder weights were recorded on days 0, 1, 3, 7, and 14. Animals were observed daily for toxic signs and morbidity. Water consumption was not monitored during this study. All in-life data was recorded using the LABCAT Body Weights Program. Rats that died during the course of this study and were not autolytic were submitted for gross necropsy.

(5) Following the 14-day study period, the rats were anesthetized with a cocktail of ketamine/acetylpromazine. Blood was collected by intracardiac puncture and the rats were euthanized using carbon dioxide. Clinical chemistry and hematology values were determined from all valid samples. The brain, heart, liver, kidneys, spleen, adrenals, thymus, epididymides/uterus, and testes/ovaries were removed and weighed for absolute organ weights, organ-to-body weight ratios, and organ-to-brain weight ratios. Gross necropsies were completed on all terminal animals. The following parameters, by test group, were analyzed and compared to the controls.

(a) Body weights

(b) Weight gains

(c) Food consumption

(d) Absolute organ weights

(e) Organ-to-body weight ratios

(f) Organ-to-brain weight ratios

(g) Hematology (Cell-Dyn 3700 Hematology Analyzer, Abbott Laboratories, Abbott Park, IL 60064): white blood cell count (WBC), WBC differential (% neutrophils (NEU %N), % lymphocytes (LYM %L), % monocytes (MONO %M), % eosinophils (EOS %E), % basophils (BASO %B)), red blood cell count (RBC), hemoglobin (HGB), hematocrit (HCT), mean cell volume (MCV), mean cell hemoglobin (MCH), mean cell hemoglobin concentration (MCHC), red blood cell distribution width (RDW), platelets (PLT), and mean platelet volume (MPV).

(h) Clinical Chemistry (VetTest 8008 Chemistry Analyzer and VetLyte Na, K, Cl Analyzer, IDEXX Laboratories, Inc., One IDEXX Drive, Westbrook, ME 04092): alkaline phosphatase (ALK P), alanine aminotransferase (ALT), aspartate aminotransferase (AST), blood urea nitrogen (BUN), calcium (Ca), cholesterol (CHOL), creatinine kinase (CK), creatinine (CREA), glucose (non-fasting) (GLU), lactate dehydrogenase (LDH), total bilirubin (TBIL), total protein (TP), triglycerides (TRIG), sodium (Na), potassium (K), and chlorine (Cl).

(6) Data from each treatment group were statistically compared to controls using a one-way analysis of variance (ANOVA) (SigmaStat for Windows®, version 3.1, SPSS, Inc.). When significance was observed, the data were further analyzed using the Holm-Sidak Method. If a normality test failed, the data was subjected to a log transformation prior to performing ANOVA. If the normality test failed again after the data was transformed, ANOVA on ranks (Kruskal-Wallis test) was performed. Statistical significance was defined at the $p \leq 0.05$ level. The results from these data were used to determine the dosage levels for the subchronic oral toxicity study.

c. Subchronic Oral Toxicity Study.

(1) A 90-day oral toxicity study was conducted in male and female rats in accordance with the USACHPPM DTOX SOP for 14-day Range Finding and 90-day Oral Toxicity Study in Rodents (reference 6).

(2) This study involved the use of 60 male and 60 female Fischer 344 rats. Following a quarantine/acclimatization period, the animals were randomly distributed using the LABCAT Randomization Program into five dose groups and one control group. All groups contained 10 animals of each sex. Dosage levels were set at 0 (negative control), 4, 8, 10, 12, and 15 mg/kg/day. A staggered start of approximately 2 weeks between males and females was used to facilitate scheduling of necropsies and week 11 observations for the Functional Observation Battery (FOB). Negative control animals were dosed with the 1% Methylcellulose/0.2% Tween 80 in distilled water diluent solution at the same volume per body weight as all other dose groups (4 ml/kg).

(3) Four rats of each sex were housed in the same animal room as study animals and used for health monitoring purposes. Two rats of each sex were shipped to Charles River Laboratories for health monitoring after the quarantine period and at the conclusion of the 90-day study to assess the general health of the purchased animals. Serology, bacteriology, pathology, and parasitology testing were performed by Charles River Laboratories.

(4) A careful clinical examination was made for each animal prior to initiation of treatment and once weekly during treatment of animals. Observations included but were not limited to changes in skin and fur, eyes, mucous membranes, occurrence of secretions and excretions, and autonomic activity (e.g., lacrimation, piloerection, pupil size, unusual respiratory pattern). Changes in gait, posture and response to handling as well as the presence of clonic or tonic movements, stereotypes (e.g., excessive grooming, repetitive circling) or bizarre behavior (e.g., self-mutilation, walking backwards) were recorded. Records indicated time of onset, degree, and duration of all signs. A scoring system for observations explicitly defined by the Toxicity Evaluation Program was used. FOB observations were made on all animals prior to the scheduled study start and once weekly until the scheduled necropsies (reference 7). Once near the end of the exposure period (not earlier than week 11), assessment of motor activity, grip strength, and sensory reactivity to stimuli of different types was conducted.

(5) The RDX suspensions and diluent control were administered daily (7 days per week, total of 90 doses) for 91 calendar days. A 16 GA x 2-inch stainless steel gavage needle was used

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to facilitate oral dosing. Each batch of suspensions that were mixed were sampled and analyzed to verify the concentrations prior to use. A 90-day stability study on a single suspension of RDX/Methylcellulose/Tween 80 in distilled water was initiated prior to beginning the ALD. This suspension was sampled and analyzed weekly for a period of approximately 90 calendar days to ensure that the dosing suspensions would remain stable throughout the 90-day study.

(6) Body weights and feeder weights were recorded on days -3, -1, 0 (first day of dosing), 7, and weekly thereafter. Doses were adjusted weekly to reflect the change in individual body weights. Animals were observed daily for toxic signs. All data were recorded using the LABCAT In-Life Program. Water consumption was not monitored during this study.

(7) Ophthalmic examinations were performed on all control and treated animals prior to the scheduled start of the 90-day study and within a week of the scheduled necropsies (reference 8). Urinalysis was also performed on 8 out of 10 animals from all dose groups (including negative control) within 2 weeks of the final (90-day) necropsies (reference 9).

(8) Following the 90-day study period, the rats were anesthetized with a cocktail of ketamine/acetylpromazine. Blood was collected by intracardiac puncture and the rats were euthanized using carbon dioxide. Clinical chemistry, hematology, and coagulation values were determined from all valid samples. The brain, heart, liver, kidneys, spleen, adrenals, thymus, epididymides/uterus, and testes/ovaries were removed and weighed for absolute organ weights, organ-to-body weight ratios, and organ-to-brain weight ratios. The tissues harvested for histopathological evaluation included the brain, pituitary, thyroid w/ parathyroid, thymus, lungs, trachea, heart, bone marrow, salivary gland, liver, spleen, kidney, adrenal, pancreas, gonads, uterus, aorta, esophagus, stomach, duodenum, jejunum, ileum, caecum, colon, urinary bladder, lymph node, peripheral nerve, thigh musculature, eye, spinal cord (three levels), and exorbital lachrymal gland. Although these tissues were harvested from all dose groups, only the control and 15 mg/kg/day tissues were sent for histopathological evaluation at this time. The following parameters, by test group, were analyzed and compared to controls.

(a) Body weights

(b) Weight gains

(c) Food consumption

(d) Absolute organ weights

(e) Organ-to-body weight ratios

(f) Organ-to-brain weight ratios

(g) Hematology (Cell-Dyn 3700 Hematology Analyzer, Abbott Laboratories, Abbott Park, Illinois 60064): white blood cell count (WBC), WBC differential (% neutrophils (NEU %N), % lymphocytes (LYM %L), % monocytes (MONO %M), % eosinophils (EOS %E), % basophils (BASO %B)), red blood cell count (RBC), hemoglobin (HGB), hematocrit (HCT),

mean cell volume (MCV), mean cell hemoglobin (MCH), mean cell hemoglobin concentration (MCHC), red blood cell distribution width (RDW), platelets (PLT), and mean platelet volume (MPV).

(h) Clinical Chemistry (VetTest 8008 Chemistry Analyzer and VetLyte Na, K, Cl Analyzer, IDEXX Laboratories, Inc., One IDEXX Drive, Westbrook, ME 04092): alkaline phosphatase (ALK P), alanine aminotransferase (ALT), aspartate aminotransferase (AST), blood urea nitrogen (BUN), calcium (Ca), cholesterol (CHOL), creatinine kinase (CK), creatinine (CREA), glucose (non-fasting) (GLU), lactate dehydrogenase (LDH), total bilirubin (TBIL), total protein (TP), triglycerides (TRIG), sodium (Na), potassium (K), and chlorine (Cl).

(i) Coagulation (MCA 210 Microsample Coagulation Analyzer, BioData Corporation, 155 Centennial Plaza, P.O. Box 347, Horsham, PA 19044): average prothombin time (AVG PT) and average activated prothombin time (AVG APTT).

(j) Urinalysis: volume, color, appearance, pH, specific gravity, glucose, bilirubin, urobilinogen, ketone, blood, protein, nitrite, and leukocytes.

(9) Statistical Analysis.

(a) Data from each treatment group were statistically compared to controls using a one-way analysis of variance (ANOVA) (SigmaStat for Windows®, version 3.1, SPSS, Inc.). When significance was observed, the data were further analyzed using the Holm-Sidak Method. If a normality test failed, the data was subjected to a log transformation prior to performing ANOVA. If the normality test failed again after the data was transformed, ANOVA on ranks (Kruskal-Wallis test) was performed. Statistical significance was defined at the $p \leq 0.05$ level.

(b) For the FOB, all analyses were performed separately for males and females. For variables that were measured as a frequency of occurrence, a Chi-square analysis was used to compare the responses across all treatment groups followed by either a Chi-square analysis or a Fisher's exact test on pairs of treatment groups if the overall test was significant. For variables that were continuous, the treatment groups and sexes were compared using a two factor analysis of variance (ANOVA) or a one factor ANOVA was used for each sex to compare the treatment groups. If the treatment groups were significantly different, then a Tukey's test was used to compare pairs of treatment groups. SPSS® 12.0 and 13.0 and Stat Xact were used to perform all analyses and statistical significance was defined as $p<0.05$ for all tests.

d. Subchronic Behavioral Testing. All rats were tested using an FOB which is consistent with the procedure outlined by Moser (reference 10). This battery consisted of weekly home cage, hand-held, open arena observations. After week 11, elicited responses and motor activity monitoring evaluations were made. A more detailed explanation of methods and procedure can be found in Appendix V.

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e. Immunotoxicity Assays.

(1) Specific measures considered to be predictive in determining immunotoxicity were integrated in a weight of evidence process as part of the 90-day study (references 11 and 12). The following were used as a basis for comparison between treatments and gender. Included were:

(a) Spleen and thymus/body weight comparisons.
(b) Cellularity of the spleen and thymus as proportion of organ weight.
(c) Proportion of cell surface markers of the spleen and thymus.
(d) Evaluation of red and white blood cell populations.

(2) Following necropsy, primary and secondary lymphoid organs (thymus and spleen) were bisected and the cells prepared according to Gogal et al. (reference 13) using half of each organ for enhanced histopathological evaluation and the remainder used for the descriptive assays (N = 98). Data from non-scheduled death animals were not collected.

(3) Briefly, whole spleen and thymus were weighed, and then bisected. Half of the organs used for the subsequent procedures were weighed and immediately placed in 15 ml centrifuge tubes on ice containing RPMI-1640 medium with glutamine (Sigma-Aldrich, St. Louis, Missouri). Cells for each tissue were liberated through gentle dissociation of the organ against a stainless steel screen using curved forceps. Cells were pipetted through the screen matrix to remove debris following dissociation. Cells were washed twice in phosphate buffered saline (PBS; Fisher Scientific, Norcross, Georgia) for 10 minutes at 250 G and 10°C. Because of the potential for interference, red blood cells were lysed from splenic preparations using a hypertonic lysing solution (ack lysis buffer) and washed again.

(4) Cells were then enumerated using a Coulter Z-1 Particle Counter (Beckman Coulter, Miami,Florida) with the discriminator set at >4μm. Cells/unit volume values were counted and thus total number cells/unit organ mass was calculated. Cell preparations were then standardized to $5 \times 10^5/100\mu l$ concentrations and aliquoted into 3 ml polypropylene tubes.

(5) Lymphocyte subpopulations were then characterized in the thymic and splenic cell preparations and evaluated according to treatment and sex. This included enumeration of B and T-cells in the spleen and CD4 / CD8 antigens of maturing lymphocytes in the thymus. Monoclonal antibodies conjugated with phycoerythrin (PE) or fluorescein isothiocyanate (FITC) were added to each sample at a concentration of 0.2 μg/μl or 0.5 μg/μl, respectively. These concentrations were attained by preparing an antibody-specific solution in PBS and dispensing in 100μl increments. Antibody/cell preparations were then incubated on ice in the dark for 30 minutes and washed again prior to analysis.

(6) Rat monoclonal antibodies specific for cell surface markers CD4 and CD8a were used for cell suspensions for the thymus (clones OX-38 and G28, respectively), and CD3 (pan thymocyte marker) and CD45-RA (B-cell) were used for the spleen cell suspensions (clones OX-52 and OX-33, respectively). Isotypic controls were R-PE conjugated mouse IgG_1,κ and IgG_{2a},κ (clones MOPC-31C and G155-178, respectively) and FITC conjugated mouse IgG_{2a},κ (clone

G155-178). All monoclonal antibodies were purchased from BD Pharmingen (San Diego, California).

(7) Analysis for cell surface markers was completed using the Coulter Epics XL/MCL Flow Cytometer (Beckman-Coulter, Miami, Florida). Gates for analysis were selected using non-stained cells and a representative sample stained with the appropriate flurochrome conjugated isotypic controls resulting in less than a 2% positive response. Isotypic controls (i.e., non-specific antibody isotypes) were used to assess the possibility of non-specific binding. Viability was assessed through a back-gating procedure dependant upon propidium iodide dye exclusion. Cell preparations were analyzed collecting 10,000 events from each sample.

(8) All data were tested with a Two-way ANOVA, using sex and treatment as variables. Tests for multiple comparisons were done using the Holm-Sidak method.

7. RESULTS.

a. Analytical Chemistry. The results of the 90-day stability study, performed by USACHPPM DLS prior to the initiation of the subchronic study, showed that RDX concentration in the dosing suspension remained within acceptable ranges for 90-days. Weekly recovery percentages ranged from 84-113% throughout the 90-day sampling period. The RDX concentration of each batch of 5 dosing suspensions (3 batches) was also verified prior to use by USACHPPM DLS. With the exception of one suspension, recovery percentages for the dosing suspensions were within acceptable ranges and varied from 83-114%. The recovery reported for the batch one, 1 mg/ml suspension (114%) was adjusted down to 100% in the LABCAT dosing program on Day 0 of the study. The analytical chemistry results are contained in Appendix D.

b. Approximate Lethal Dose.

(1) The ALD data are presented in Appendix E. The oral ALD was estimated to be 68 mg/kg for both male and female rats.

(2) The earliest toxic signs, tremors and convulsions, appeared within 17-32 minutes in male rats, and within 15-29 minutes in female rats that received 152 mg/kg of the RDX suspension or higher. All male and female rats dosed with 45 mg/kg or greater of the RDX suspensions experienced tremors and convulsions within 3 hours of dosing. The majority of the male rats within the top 5 dose groups and the female rats within the top 3 dose groups exhibited increased salivation following the onset of convulsions. All male rats receiving a dose of 68 mg/kg or greater died within 3 hours of dosing, with the exception of the rat receiving 228 mg/kg which died on day 2 of the recovery period. All female rats receiving a dose of 68 mg/kg or greater died within 2.5 hours of dosing, with the exception of the rat receiving 101 mg/kg which died on day 1 of the recovery period. Gross pathology of all animals that died on study showed that a majority of the animals had staining around the mouth and nose. In addition, 2 rats exhibited areas of lung consolidation (white spots) and 2 rats appeared to have red blotches on the lungs. Gross pathology observations in surviving animals were unremarkable.

c. 14-Day Oral Repeated Dose Toxicity Study.

(1) A summary of results and raw data for the 14-day oral repeated dose toxicity study are presented in Appendices F-K.

(2) Neuromuscular signs (tremors, convulsions) as well as pre-term deaths were observed in all male dose groups at 17 mg/kg and above. Additional observations noted throughout the highest 4 dose groups included blood stains around the mouth and nose and low arousal. No toxic signs were observed in any of the male dose groups below 17 mg/kg. Body weights were significantly lower in male animals exposed to 34 and 42.5 mg/kg/day on day 1 and 17 and 34 mg/kg/day on day 7 as compared to controls. Body weight changes were significantly decreased in male rats receiving 17, 25.5, 34, and 42.5 mg/kg/day on days 0-1 when compared to controls. On days 1-3, male body weight changes were significantly decreased in dose groups receiving 8.5, 17, 25.5, and 34 mg/kg/day as compared to controls. Food consumption was significantly lower during days 0-7 in male rats receiving 8.5, 17, 25.5, and 34 mg/kg/day as compared to controls.

(3) Neuromuscular signs were observed in all female dose groups at 17 mg/kg and above. Pre-term deaths occurred at dosage levels of 25.5 mg/kg and above. Additional clinical signs observed in the highest four dose groups include high arousal, blood around the mouth and nose, barbering, and lacrimation. No toxic signs were observed in any of the female dose groups below 17 mg/kg. Body weights were significantly lower in female rats exposed to 34 mg/kg/day on day 1 and in female rats exposed to 8.5 mg/kg/day on day 14, when compared to controls. Female body weight gains were significantly lower in the 25.5, 34, and 42.5 mg/kg/day dose groups for days 0-1 and in the 17 mg/kg/day dose group for days 1-3. The female 17 and 25.5 mg/kg/day dose groups had significantly higher body weight gains for days 7-14 as compared to controls. Food consumption for days 0-7 was significantly lower in female rats exposed to 8.5, 17, and 25.5 mg/kg/day as compared to controls. Absolute liver weights and liver-to-brain weight ratios were significantly decreased in female rats dosed with 8.5 mg/kg/day.

(4) Cholesterol was significantly elevated in surviving female rats in the 8.5 mg/kg/day dose group.

(5) The results of gross pathological examination of both sexes noted signs of bloody discharge around the mouth and nose, hemorrhagic thymus and lungs, petechiation of thymus, and an accessory spleen. This was observed primarily in the male higher dose groups (17 mg/kg/day and higher.

(6) Based upon the results of this 14-day oral repeated dose study, 15 mg/kg/day was selected as the highest dosing level for the 90-day subchronic study.

d. Subchronic Oral Toxicity Study.

(1) Charles River Laboratories screened eight animals, not randomly chosen for this study but housed in the same room, for serology, bacteriology, pathology, and parasitology. Two rats of each sex were shipped to Charles River Laboratories for health monitoring prior to the study

start date and after the last dosing day. The results of the pre-study evaluation showed the animals to be in good health with the exception of one rat that exhibited a minimal growth of the bacteria *Staphylococcus aureus* (reference 14). These bacteria are typically found in the nasal membranes of warm-blooded animals and are not considered a primary pathogen of immunocompetent animals. The results of the post-study evaluation revealed one rat with a minimal growth of the bacteria *Staphylococcus aureus* and three rats that were polymerase chain reaction positive for the *Helicobacter genus*. All other health monitoring parameters were within normal limits (reference 14).

(2) Ophthalmic examinations were performed on all animals prior to the scheduled start of the 90-day study and within a week of the scheduled necropsies. All observations prior to study initiation were within normal limits with the exception of two rats that had strands of pigment in the cornea. Observations taken within a week of the scheduled necropsies revealed two rats with mild cataracts and three different rats with either discoloration of the fundus, diffuse corneal opacity, or pale vessels in the fundus. These observations are relatively common in Fischer 344 rats at 4 months of age and should not be attributed to the administration of the test compound.

(3) Male and female unscheduled deaths occurred in all of the dose groups with the exception of the control and 4 mg/kg groups (Table 2). Pre-term deaths occurred at a higher frequency and earlier in the study within the highest three dose groups. In almost all cases, these deaths were preceded by convulsions. Gross necropsies were performed on all unscheduled deaths that were not determined to be autolytic. Findings noted during these necropsies included three rats with lungs that were dark red in color, three rats with staining around the mouth and nose, and two rats with livers that were dark red and mottled. These findings occurred in both the male and female 10 and 12 mg/kg/day dose groups.

TABLE 2
PRE-TERM DEATHS

Dose Group (mg/kg)	Surviving Males/Total	Surviving Females/Total
0	10/10	10/10
4	10/10	10/10
8	9/10	9/10
10	7/10	8/10
12	8/10	5/10
15	7/10	6/10

(4) Transient clinical signs noted for some animals in this study were considered to be treatment-related. Observations included changes in arousal, blepharosis, increased salivation, blood stains around the mouth and nose, rough haircoat, tremors, and convulsions (Appendix L). The higher dosage groups showed more of these signs with greater severity than the lower dosage animals. Neuromuscular signs appeared in the higher dosage groups during the first week of dosing and persisted in surviving animals throughout the 90-day study. Other signs, such as alopecia and congested breathing, were noted on occasion throughout the study in animals from all dose groups, but were not considered to be treatment-related.

e. 90-Day Results.

(1) Examination of urine samples taken within one week prior to necropsy revealed no significant changes in specific gravity or pH. Urine volume was significantly increased in female rats dosed with 12 and 15 mg/kg/day (Appendix M). No distinct dose related trends were observed in glucose, bilirubin, ketone, blood, protein, urobilinogen, nitrite, or leukocytes.

(2) Table 3 provides a summary of significant male and female body weights, body weight gains, and food consumption throughout the 90-day study.

TABLE 3
SUMMARY OF OBSERVED STATISTICAL SIGNIFICANCE

	Male Dose Groups			Female Dose Groups		
	Body Weights	Food Consumption	Body Weight Gain	Body Weights	Food Consumption	Body Weight Gain
Days 0-7		(-) 8, 10, 12, 15	(-) 8, 10, 12, 15	(-) 12, 15	(-) 8, 10, 12, 15	(-) 10, 12, 15
Days 7-14	(-) 8, 10, 15	(-) 8, 10, 15				(+) 12, 15
Days 14-21	(-) 8, 10					
Days 21-28	(-) 8, 10, 12	(-) 8, 10, 12			(+) 15	(+) 15
Days 28-35	(-) 8, 10, 12	(-) 8, 12		(+) 15	(+) 15	(+) 15
Days 35-42	(-) 8, 10, 12	(-) 8, 12		(+) 15	(+) 15	(+) 10, 15
Days 42-49	(-) 8	(-) 8, 12		(+) 15	(+) 15	(+) 12, 15
Days 49-56	(-) 8	(-) 8		(+) 15	(+) 15	
Days 56-63			(+) 10, 12	(+) 15	(+) 15	
Days 63-70			(+) 12, 15	(+) 12, 15	(+) 12	
Days 70-77				(+) 8, 10, 12, 15	(+) 12, 15	
Days 77-84		(+) 15		(+) 12, 15	(+) 10, 12, 15	
Days 84-91	(-) 8			(+) 10, 12, 15	(+) 10	

(-) = significantly reduced vs. controls
(+) = significantly increased vs. controls

(3) Group summaries of body weights, food consumption, food efficiency, body weight gains, organ weights, organ weight ratios, clinical chemistry and hematology are provided in Appendices N-T. Individual animal data for body weights, food consumption, food efficiency, body weight gains, organ weights, organ weight ratios, clinical chemistry and hematology are also included in Appendices N-T. A summary of the histopathological findings as well as a copy of the histopathology report is furnished in Appendix U.

(4) FOB data and summary are provided in Appendix V.

(5) Necropsy was performed on surviving male and female rats from each dosage and control group on Day 91 or 92 of the study. Clinical chemistry, hematology, organ weight, and histopathology data were collected for each animal.

(6) Brain weights were significantly increased in males that received 12 mg/kg/day and 15 mg/kg/day. Testes-to-body weight ratios were significantly decreased in males dosed with 15 mg/kg/day. Testes-to-brain weight ratios were significantly decreased in males that received either 10, 12, or 15 mg/kg/day as well as epididymus-to-brain weight ratios in males receiving 8, 12, or 15 mg/kg/day. Body weights and spleen weights were significantly increased in females receiving 10, 12, or 15 mg/kg/day. Kidney and liver weights were significantly increased in females receiving 10 or 15 mg/kg/day. Brain-to-body weight ratios were significantly reduced in female rats dosed with either 10, 12, or 15 mg/kg/day. Female heart-to-body and kidney-to-body weight ratios were significantly reduced in the 15 mg/kg/day dose group. Female kidney-to-brain and liver-to-brain weight ratios were significantly increased in the 10 mg/kg/day and 15 mg/kg/day dose groups, respectively. Female spleen-to-brain weight ratios were significantly increased in both the 10 mg/kg/day and 15 mg/kg/day dose groups.

(7) A significant increase in MCV was noted in male rats exposed to 8, 10, or 12 mg/kg/day, as compared to controls. A significant increase in MCV was also observed in female rats dosed with 10 or 12 mg/kg/day.

(8) Clinical chemistry analysis revealed CHOL was significantly decreased in male rats dosed with 8, 10, 12, or 15 mg/kg/day, as compared to controls. Female clinical chemistry analysis did not exhibit any significant differences between the treated and control groups.

(9) "All histopathologic findings in terminal sacrifice animals were considered to be incidental findings, part of spontaneous disease processes or related to some aspect of experimental manipulation other than administration of the test article. There was no treatment-related alteration in the incidence, severity or histologic character of those spontaneous and incidental histologic findings." (reference 15, Appendix U)

(10) "Subacute inflammation of the larynx consisted of lymphocytic infiltration in the laryngeal mucosa. Occurrence of laryngitis in 2/7 terminal sacrifice males from the 15 mg/kg group was viewed with interest, but the low incidence, absence of the finding in females, and known common occurrence of such findings as part of spontaneous disease processes suggested the laryngitis seen in males in the study was an incidental finding." (reference 15, Appendix U)

(11) "The liver of one female from the 15 mg/kg group had a moderate-sized focus of basophilic cytoplasmic alteration. The lesion resulted in no compression of surrounding hepatic parenchyma. Affected hepatocytes were slightly larger than hepatocytes in surrounding normal parenchyma, but there was no other evidence of atypism. Occurrence of this lesion in a high-dose female was viewed with interest, but the low incidence of a singular lesion coupled with the known common occurrence of such spontaneous lesions precluded a determination that the focal basophilic cytoplasmic alteration was related to administration of the test article." (reference 15, Appendix U)

(12) "Mild subacute inflammation of the prostate was present in 1/7 terminal sacrifice males from the 15 mg/kg group. The lesion consisted of an infiltration of lymphocytes, plasma cells and neutrophils into the interstitium of the prostate gland. Inflammatory lesions of this type are seen with some frequency in the prostate gland of laboratory rats, and are thought to be

associated with infectious disease processes. Occurrence of one such lesion in a high-dose male from the present study was considered to be within the expected incidence level. (reference 15, Appendix U)

(13) Administration of 1,3,5-trinitro-1,3,5-triazine (RDX) to Fischer 344 rats for 90 days via oral gavage at a dosage level of 15 mg/kg was associated with no treatment-related histologic alterations. Three of ten males and four of ten females from the 15 mg/kg group died prior to the scheduled terminal sacrifice. Tissues were collected for histologic examination from only one of these decendent males, therefore it was not possible to determine treatment-related histologic alterations in the majority of the decendent rats. Histologic alterations in the single decendent rat suggested terminal cardiovascular dysfunction, but did not indicate a specific underlying lesion." (reference 15, Appendix U)

f. Functional Observation Battery. The FOB was used to measure the behavioral effects of RDX. The FOB was conducted weekly, and measurements were recorded for each animal with the observer being blinded to the treatment group. Measurements were made on hand held observations, open arena observations, motor activity, and home cage observations. Statistical analyses were conducted separately for male and female animals using either Chi-square tests on categorical data or ANOVA on continuous type data ($p< 0.05$). A complete list of statistically significant differences appears in the neurotoxicity report found in Appendix V. Sporadic statistical significance was noted in many parameters, but no patterns or biological meanings can be derived from the results except the following:

(1) The frequency of abnormal skin appearance (i.e., stained haircoat) during week 12 was significantly greater in the female 15 mg/kg/day dose group as compared to controls.

(2) The presence of barbering was significantly greater in the female 15 mg/kg/day dose group compared to controls during weeks 9 and 12.

g. Immunotoxicity Assays.

(1) Mean half spleen/whole spleen ratios were 0.49 ± 0.02 and 0.55 ± 0.02 for the males and females, respectively. Mean ratios for the thymus were 0.47 ± 0.01 and 0.48 ± 0.01 for males and females, respectively. Mean cell viability for the cell preparations were > 84% and > 70% for the thymic and splenic preparations, respectively.

(2) No statistical differences were found between any of the treatments and control for the spleen and thymus percent body weight ratios (Appendix R, Tables R-3 and R-4).

(3) There were no treatment-related differences in the number of cells/μg organ mass for the spleen or thymus ($P > 0.07$; Appendix W, Table W-1). There were differences between sexes ($P < 0.001$) where females had a greater number of cells/organ mass for both thymus and spleen.

(4) Mean values for CD4/CD8 markers and T-cell and B-cell proportions are presented in Appendix W, Tables W-2 and W-3. No significant differences or trends were apparent as a

result of treatment. However, there were differences between males and females in B- and T-cell proportions and in relative proportions of CD4+CD8- and CD4-CD8- populations. There were no significant interactions between gender and treatment for any comparison.

(5) Thymic and splenic cellular surface marker proportions were roughly consistent with those reported elsewhere in the rat (references 13, 16, 17, 18, and 19). Some of this variation may be due to differences between clones used in this present study and those reported elsewhere (references 13, 16, 17, 18, and 19). Additionally, no dose-related trends were evident in any of the surface markers evaluated. Representative profiles of the thymic and splenic cell surface marker assays are provided in Appendix W, Figure 1. All data are presented as mean values with standard errors of the mean in Appendix W.

8. DISCUSSION.

a. The administration of RDX to male and female Fischer 344 produced pre-term deaths at dosage levels of 8, 10, 12, and 15 mg/kg/day. Nearly all observed pre-term deaths were preceded by neurotoxic signs such as tremors and convulsions. Female rats appeared to be slightly more susceptible to neurotoxic signs than male rats. Eighty to 90% of male and female rats exhibited neurotoxic signs in the 12 and 15 mg/kg/day dose groups beginning on day 0 of the study and persisting throughout the 90-day period. The percentage of rats experiencing convulsions in the 8 and 10 mg/kg/day dose groups dropped to 20-30% and 40-50%, respectively. No changes associated with the compound administration were noted in central nervous system tissues in the histopathology report.

b. Additional signs attributed to the administration of RDX included changes in arousal, blepharosis, and bleeding from the mouth and nose. Observations of salivation, stained haircoat, and congested breathing occurred sporadically throughout the dose groups. These observations could be considered signs of toxicity (and/or stress) or more likely related to the oral dosing procedure. Other signs, such as barbering and diarrhea, were noted on occasion in animals from all dose groups but were not considered to be signs of toxicity.

c. Urine volume was significantly increased in female rats receiving 12 and 15 mg/kg/day. This finding is believed to be more related to the palatability of the suspension being administered rather than a treatment related finding since the higher dose animals were frequently observed drinking immediately following dosing. The male rats in the higher dose groups also produced slightly higher, but non-significant, urine volumes compared to the lower dose groups and controls.

d. Table 3 provides an overview of statistical significance observed in the male and female body weights, body weight gains, and food consumption. In general, male and female food consumption and body weight gains were significantly decreased in the highest 4 dose groups during the first week. Male rats in the higher dose groups continued to have decreased food consumption, as well as corresponding decreased body weights, throughout the first half of the study. Although this significance was observed in the higher dose groups, it was more likely a secondary effect of the compound administration (i.e., stress associated with the central nervous system effects, palatability of the test compound) rather than a direct toxic effect.

Histopathology results did not show any gastrointestinal abnormalities in the male 15 mg/kg/day dose group. With the exception of the first week of the study (8 and 15 mg/kg/day dose groups significantly lower vs. controls), male food efficiency calculations did not show any significance throughout the first half of the study. Food efficiency in the male 10 and 12 mg/kg/day dose groups was occasionally significantly elevated versus controls during the second half of the study. Female body weights and food consumption were significantly elevated in the 15 mg/kg/day dose group for Days 28-84. The female 8, 10, and 12 mg/kg/day dose groups showed occasional significant increases in body weights and food consumption throughout the last 3 weeks of the study. Female food efficiency calculations revealed that the 12 and 15 mg/kg/day dose groups were significantly lower than controls during week 1 and significantly higher versus controls during week 2. The female 15 mg/kg/day dose group remained significantly higher than controls for Days 21-42 with the 10 mg/kg/day dose group being significantly elevated for Days 35-42 and the 12 mg/kg/day dose group being significantly elevated for Days 42-49. As with the males, significant changes in female body weights, food consumption, and body weight gains were not considered to be directly related to compound toxicity since the histopathology results revealed no gastrointestinal abnormalities in the high dose group.

e. Absolute brain weights were significantly elevated in male rats receiving 12 and 15 mg/kg/day. No changes associated with the administration of RDX were noted in the brain tissues in the histopathology report (control and 15 mg/kg only) (reference 15, Appendix U). Brain-to-body weight ratios were significantly reduced in female rats receiving 10, 12, and 15 mg/kg/day. This was not necessarily considered a treatment related finding since female absolute body weights were significantly elevated in the same dose groups.

f. Testes-to-body weight ratios were significantly decreased in high dose males and testes-to-brain weight ratios were significantly decreased in males receiving 10, 12, and 15 mg/kg/day. Absolute testes weights in the 15 mg/kg/day dose group were slightly decreased, although not significantly, compared to the other dose groups and controls. In addition, absolute brain weights in the 10, 12, and 15 mg/kg/day dose group were insignificantly elevated contributing to the results seen in the testes weight ratios. Histopathology revealed that "one testis of one rat from the 15 mg/kg group had moderate hypospermatogenesis, consisting of a reduction in the population of spermatogenic cellular elements." (reference 15, Appendix U) The lesion was not considered to be associated with the administration of the test article because it is a common incidental finding in laboratory rats and was limited to only one testis. Epididymus-to-brain weight ratios were significantly decreased in male rats receiving 8, 12, and 15 mg/kg/day. Histopathology results showed one high dose male with "subacute inflammation in the epididymis consisting of lymphocytic infiltration in the interstitium of the epididymis. Minor inflammatory cell infiltrations are seen with some frequency in the epididymis of rats, but are of uncertain pathogenesis." (reference 15, Appendix U)

g. Female spleen, kidney, and liver weights, as well as the weight ratios, were significantly elevated throughout the 10, 12, and 15 mg/kg/day dose groups. Hepatomegaly was seen in both the 10 and 15 mg/kg/day female dose groups. Hypocholesterolemia was significant in male rats exposed to 8, 10, 12, and 15 mg/kg/day. Histopathology of the 15 mg/kg/day dose group revealed one male rat with mild liver congestion and one female rat with a moderate-sized focus of basophilic cytoplasmic alteration (reference 15, Appendix U). Neither finding was attributed

to the administration of the test compound. Kidney weights were significantly increased in female rats receiving 10 and 15 mg/kg/day, as well as female kidney-to-body weight ratios in the 15 mg/kg/day dose group and kidney-to-brain weight ratios in the 10 mg/kg/day dose group. Absolute spleen weights were significantly increased in females receiving 10, 12, and 15 mg/kg/day. Spleen-to-brain weight ratios were significantly increased in the 10 and 15 mg/kg/day dose groups. No RDX-induced renal damage or splenic lesions were noted during the necropsies or in the histopathology report (reference 15, Appendix U). Other than the identification of the kidneys and spleen as possible target organs, the physiological implications of the increased weights and weight ratios are inconclusive.

h. The female skin or fur appearance observations showed that the 15 mg/kg/day females had statistically significant effects (week 12) resulting from the oral administration of RDX. Typically, excessive salivation and/or bleeding from the mouth was observed following the seizures or convulsions caused by the RDX. The significant increase in barbering in the 15 mg/kg/day females during weeks 9 and 12 also indicate possible compound-related effects. Overall, the higher-dose animals exhibited more "nervous behavior" throughout the study, compared to low-dose and control animals. Barbering was also observed with increased frequency in the higher-dose male rats, although not significantly.

i. Statistical differences were also noted sporadically in many of the remaining FOB and behavioral parameters. There were no patterns associated with these differences and the results do not appear to have any biological significance.

j. Immunotoxicity studies indicated that no adverse immunological effects occurred as a result of 90-day oral exposure to RDX.

9. CONCLUSIONS.

a. RDX administered orally 7 days per week for 90 days induced lethality at dosages of 8 mg/kg/day and higher in both male and female rats. Visible signs of toxicity in the 8, 10, 12, and 15 mg/kg/day dose groups included changes in arousal, blepharosis, increased salivation, blood stains around the mouth and nose, rough haircoat, tremors, and convulsions.

b. Measured signs of toxicity included alterations in brain, testes, epididymus, body, spleen, kidney, and liver weights and weight ratios, as well as urine production. Alterations in hematology and clinical chemistry also occurred. Histopathology performed on collected tissues from the control and 15 mg/kg/day dose groups revealed no treatment-related alterations. All visible and measured signs of toxicity were confined to dose groups that also produced lethality.

c. Immunotoxicity studies indicated that no adverse immunological effects occurred as a result of 90-day oral exposure to RDX.

d. The NOAEL for subchronic oral exposure to RDX for 90-days, as determined from this study, is 4 mg/kg/day based on lethality.

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APPENDIX A

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APPENDIX B

U.S. ARMY CENTER FOR HEALTH PROMOTION AND PREVENTIVE MEDICINE STRATEGIC INITIATIVES OFFICE, QUALITY ASSURANCE TEAM

Quality Assurance Statement

For: Toxicological Study No. 85-MA-5131-02, Protocol No. 5131-38-02-12-01, titled "Subchronic Oral Toxicity of RDX in Rats".

During the 90-day study, the Quality Assurance Team audited the following critical phases:

Critical Phase Audited (SIO Checklist #)	*Date Audited*	*Date Reported to Mngmt.*
1) Necropsy		
a. General Requirements (SIO #7.1)	02/09/05	03/04/05
b. Necropsy Procedures (SIO #7.2)	02/09/05	03/04/05
c. Solutions and Reagents (SIO #4.4)	02/09/05	03/04/05
d. Necropsy Records (SIO #7.5)	02/09/05	03/04/05

During the 14-day study, the Quality Assurance Team audited the following critical phases:

Critical Phase Audited (SIO Checklist #)	*Date Audited*	*Date Reported to Mngmt.*
1) Necropsy		
a. General Requirements (SIO #7.1)	09/30/04	10/08/04
b. Necropsy Procedures (SIO #7.2)	09/30/04	10/08/04
c. Solutions and Reagents (SIO #4.4)	09/30/04	10/08/04
d. Necropsy Records (SIO #7.5)	09/30/04	10/08/04
2) Analytical Chemistry Support (DLS)		
a. Test Article Receipt	09/13/04	09/29/04
b. Test Article Control	09/13/04	09/29/04

During the ALD study, the Quality Assurance Team audited the following critical phases:

Critical Phase Audited (SIO Checklist #)	*Date Audited*	*Date Reported to Mngmt.*
1) Test Systems		
a. Facilities (SIO #4.1)	09/01/04	09/29/04
b. Identification (SIO #4.3)	09/01/04	09/29/04
c. Husbandry (SIO #4.4)	09/01/04	09/29/04
d. Food and Water Supply (SIO #4.6)	09/01/04	09/29/04

U.S. ARMY CENTER FOR HEALTH PROMOTION AND PREVENTIVE MEDICINE
STRATEGIC INITIATIVES OFFICE, QUALITY ASSURANCE TEAM

Quality Assurance Statement (cont)

Critical Phase Audited (SIO Checklist #)	***Date Audited***	***Date Reported to Mngmt.***
2) Test Article (Controls)		
a. Facilities (SIO #5.1)	09/01/04	09/29/04
b. Preparation (SIO #5.4)	09/01/04	09/29/04
c. Handling (SIO #5.5)	09/01/04	09/29/04
3) Analytical Chemistry Support (Initial drying, homogenizing, weighing, mixing, and transferring) (SIO #18.1)	08/26/04	09/29/04
4) Analytical Chemistry Support (Concentration and Stability Analysis of RDX in DLS)	09/07/04	09/29/04

At the end of the study, the Quality Assurance Team audited the following critical phases:

Critical Phase Audited (SIO Checklist #)	***Date Audited***	***Date Reported to Mngmt.***
1) Final Study Report Review (SIO # 13.26)	04/10/06	04/10/06
2) Study Raw Data Review, Records and Specimen Storage, and Archiving (SIO # 14.2)	04/12/06	04/12/06

- Any findings made during the audits were made known at the time of the audit to the Study Director.

Michael P. Kefauver
GLP Assessor, SIO-QAT

APPENDIX C

ARCHIVES AND STUDY PERSONNEL

1. ARCHIVES

a. All raw data, documentation, records, protocol, and a copy of the final report generated as a result of this study will be archived in the storage facilities of the Toxicology Directorate, USACHPPM, for a minimum of five (5) years following submission of the final report to the Sponsor. If the report is used to support a regulatory action, it shall, along with all supporting data, be retained indefinitely.

b. Records on animal receipt, diet, and facility environmental parameters will be archived by the Veterinary Medicine Division, Toxicology Directorate, for a minimum of five (5) years following submission of the final report to the sponsor. If the report is used to support a regulatory action, it shall, along with all supporting data, be retained indefinitely.

c. The USACHPPM Toxicology Study No. 85-MA-5131-02 is an administrative designator used to identify funding sources only. The present studies used the Protocol No. 5131-38-02-12-01 for identification and archiving purposes.

d. The protocol, raw data, summary data, and the final report pertaining to this study will be physically maintained within Building E-2100, USACHPPM. These data may be scanned to a computer disk. Scanned study files will be stored electronically in Room 3027, Building E-2100, USACHPPM, APG, MD 21010.

e. Archived SOP's may be found in Room 1026, Building E-2100, USACHPPM, APG, MD 21010.

f. Records on animal receipt, diet, and environmental parameters are maintained in Room 3014, Building E-2100, USACHPPM, APG, MD 21010.

g. Wet tissues are stored in cage 12 of Building E-1958, APG, MD 21010.

h. Histology slides, paraffin blocks, and hematology slides are stored in the basement of Building E-1570, APG, MD 21010.

i. Archivist: Mark Michie, Biologist, Toxicity Evaluation Program

2. PERSONNEL.

a. Management: James Boles, DVM, LTC, VC, Director of Toxicology; Glenn Leach, Program Manager, Toxicity Evaluation Program (TEP).

b. Study Director: Dr. Michael Major, Program Manager, Health Effects Research Program (HERP).

c. Principal Investigator: Lee Crouse, Biologist, TEP.

d. Quality Assurance: Michael P. Kefauver, Chemist, Strategic Initiatives Office.

e. Veterinary Support, Necropsies, Ophthalmic Examinations, and Animal Care: James Boles, DVM, LTC, VC, Director of Toxicology; Ann Schiavetta, DVM, MAJ, VC, TEP; Dr. Wilfred McCain, Toxicologist, TEP.

f. Behavioral (FOB, Neurotoxicity): Heidi Paulus, Biologist, TEP.

g. Hematology, Clinical Chemistry: Matthew Bazar, Biologist, TEP; Jamie Suski, Biologist, TEP; Amy Hess-Ruth, Biologist, TEP.

h. Computer Software Support: Martha Thompson, Data Acquisition Specialist, TEP.

i. Animal Care: Terry Hanna, TEP; Richard Arnold, TEP; Robert Sunderland, TEP.

j. In-Life Support: Mark Michie, Biologist, TEP; Dr. Wilfred McCain, Toxicologist, TEP; Jeff Bergmann, Biologist, TEP; Amy Hess-Ruth, Biologist, TEP; Heidi Paulus, Biologist, TEP; John Houpt, Biologist, TEP; Jamie Suski, Biologist, TEP; Matthew Bazar, Biologist, TEP.

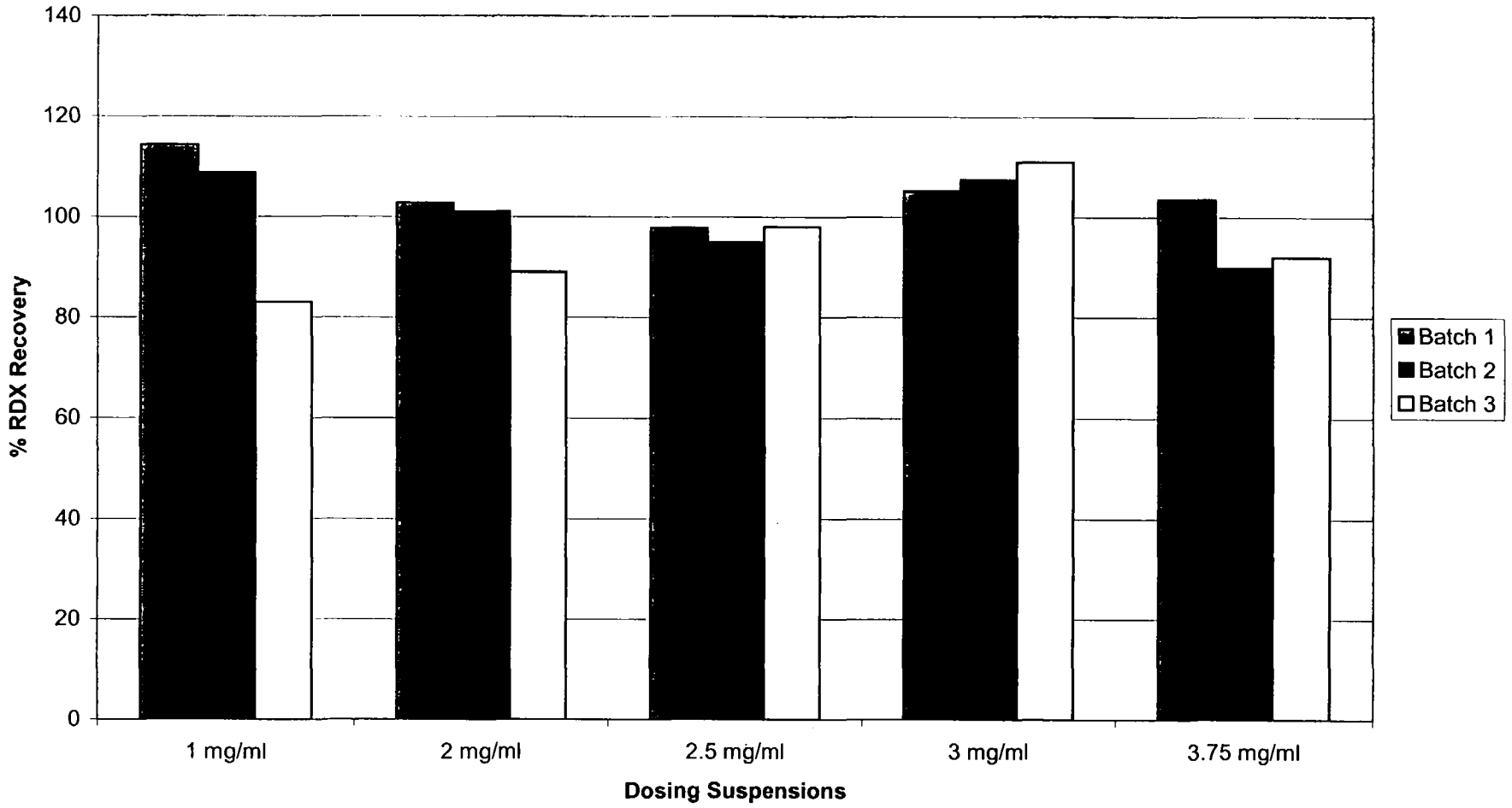
k. Pathology Laboratory Coordinator: Patricia Beall, Biologist, TEP.

APPENDIX D

ANALYTICAL CHEMISTRY
CONCENTRATION VERIFICATION AND STABILITY DATA

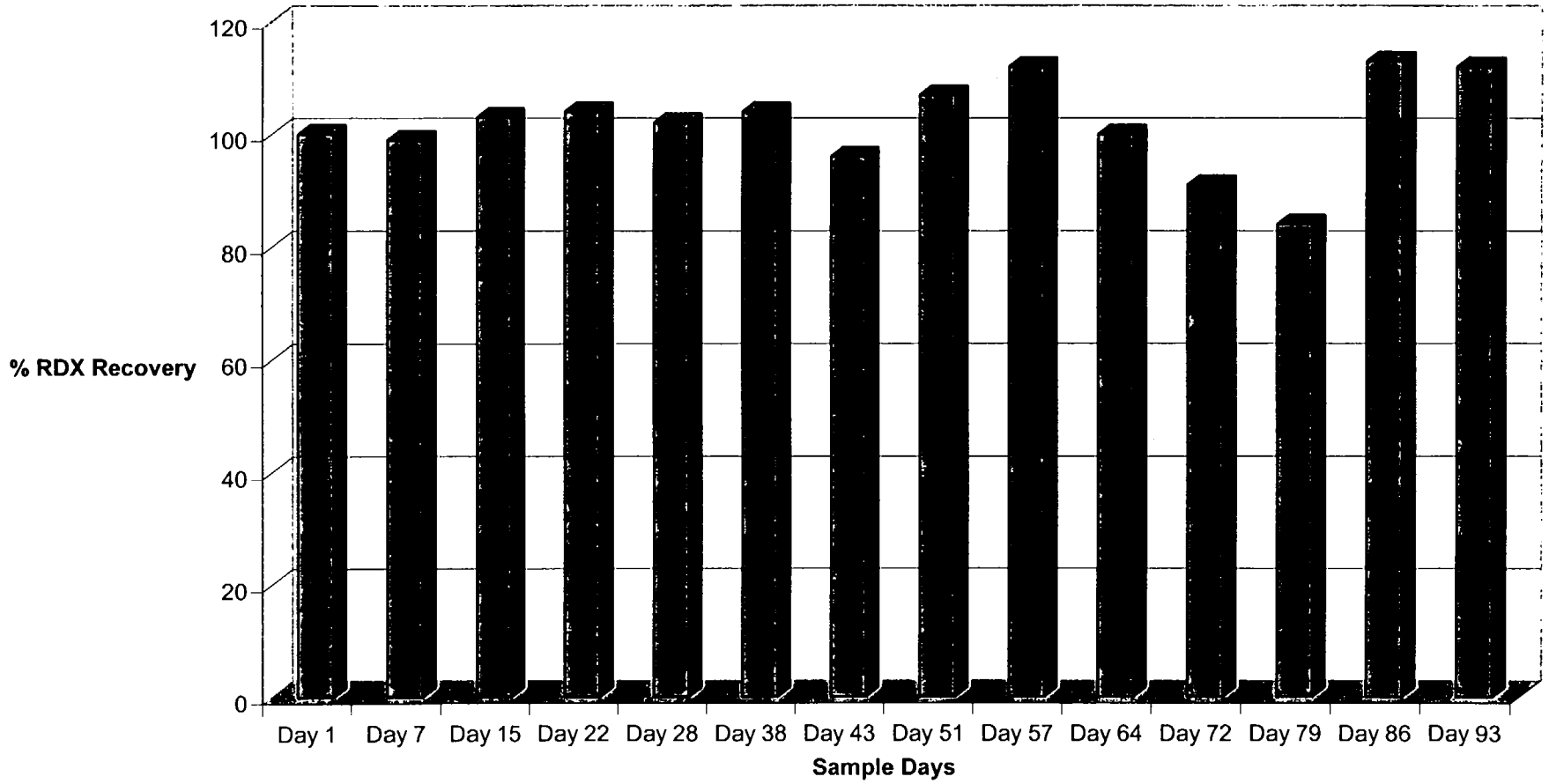
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Dosing Suspension Concentration Verifications



Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Suspension Stability



APPENDIX E
APPROXIMATE LETHAL DOSE (ALD); ORAL, RAT

Study No.: 85MA5131-02 **Protocol No.:** 5131-38-02-12-01 **SOP No.:** 17-04
Chemical Substance: RDX Lot No. 0858500 Batch No. 01B-012
Route: Oral **Species:** Fischer 344 Rat **Sex:** Male
Concentration of Test Substance: (4 suspensions) 23.75 mg/ml[A], 52.8 mg/ml[B], 107.5 mg/ml[C], and 217.25 mg/ml[D]
Diluent: 1% Methylcellulose / 0.2% Tween 80 in distilled water

INDIVIDUAL ANIMAL EFFECTS

Animal No.	Weight kg	Dose mg/kg	Volume mL	Effect S* - min to onset	Recovery min	Death min
162	0.109	Control	0.179			
163	0.098	20	0.083[A]			
164	0.098	30	0.124[A]			
165	0.117	45	0.100[B]	S2-74 min	180 min	
166	0.100	68	0.129[B]	S1-22 min; S2-32 min; S3-45 min; S6-51 min S4-51 min		172 min
167	0.104	101	0.098[C]	S2-24 min; S6-70min		124 min
168	0.108	152	0.153[C]	S1-17 min; S2-21 min		50 min
169	0.099	228	0.103[D]	S1-32 min; S2-44 min		Day 2 of recovery
170	0.108	342	0.179[D]	S1-20 min; S2-27 min; S3-36 min; S4-37 min		40 min

* Signs: S1 - tremors S2 - convulsions S3 - collapse S4 - bloody eyes S6 - salivation

Study Conclusions: ALD (mg/kg): 68 EPA Toxicity Category: II

APPENDIX E
APPROXIMATE LETHAL DOSE (ALD); ORAL, RAT

Study No.: 85MA5131-02 **Protocol No.:** 5131-38-02-12-01 **SOP No.:** 17-04
Chemical Substance: RDX Lot No. 0858500 Batch No. 01B-012
Route: Oral **Species:** Fischer 344 Rat **Sex:** Female
Concentration of Test Substance: (4 suspensions) 23.75 mg/ml[A], 52.8 mg/ml[B], 107.5 mg/ml[C], and 217.25 mg/ml[D]
Diluent: 1% Methylcellulose / 0.2% Tween 80 in distilled water

INDIVIDUAL ANIMAL EFFECTS

Animal No.	Weight kg	Dose mg/kg	Volume mL	Effect S* - min to onset	Recovery min	Death min
222	0.095	Control	0.151			
223	0.096	20	0.081[A]			
224	0.092	30	0.116[A]			
225	0.096	45	0.082[B]	S2-45 min	Day 2 of recovery	
226	0.095	68	0.122[B]	S2-34 min		151 min
227	0.099	101	0.093[C]	S1-40 min; S2-49min		Day 1 of recovery
228	0.094	152	0.133[C]	S1-28 min; S2-29 min		65 min
229	0.097	228	0.102[D]	S1-23 min; S2-24 min; S7-49 min		86 min
230	0.096	342	0.151[D]	S2-15 min; S1-16 min; S4-28 min; S6-36 min S7-39 min		57 min

* Signs: S1 - tremors S2 - convulsions S3 - bloody eyes S4 - collapse S6 - strob tail S7 - salivation

Study Conclusions: ALD (mg/kg): 68 EPA Toxicity Category: II

APPENDIX F

SUMMARY OF 14-DAY BODY WEIGHTS AND INDIVIDUAL BODY WEIGHT DATA

Appendix F
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

14-Day Body Weights

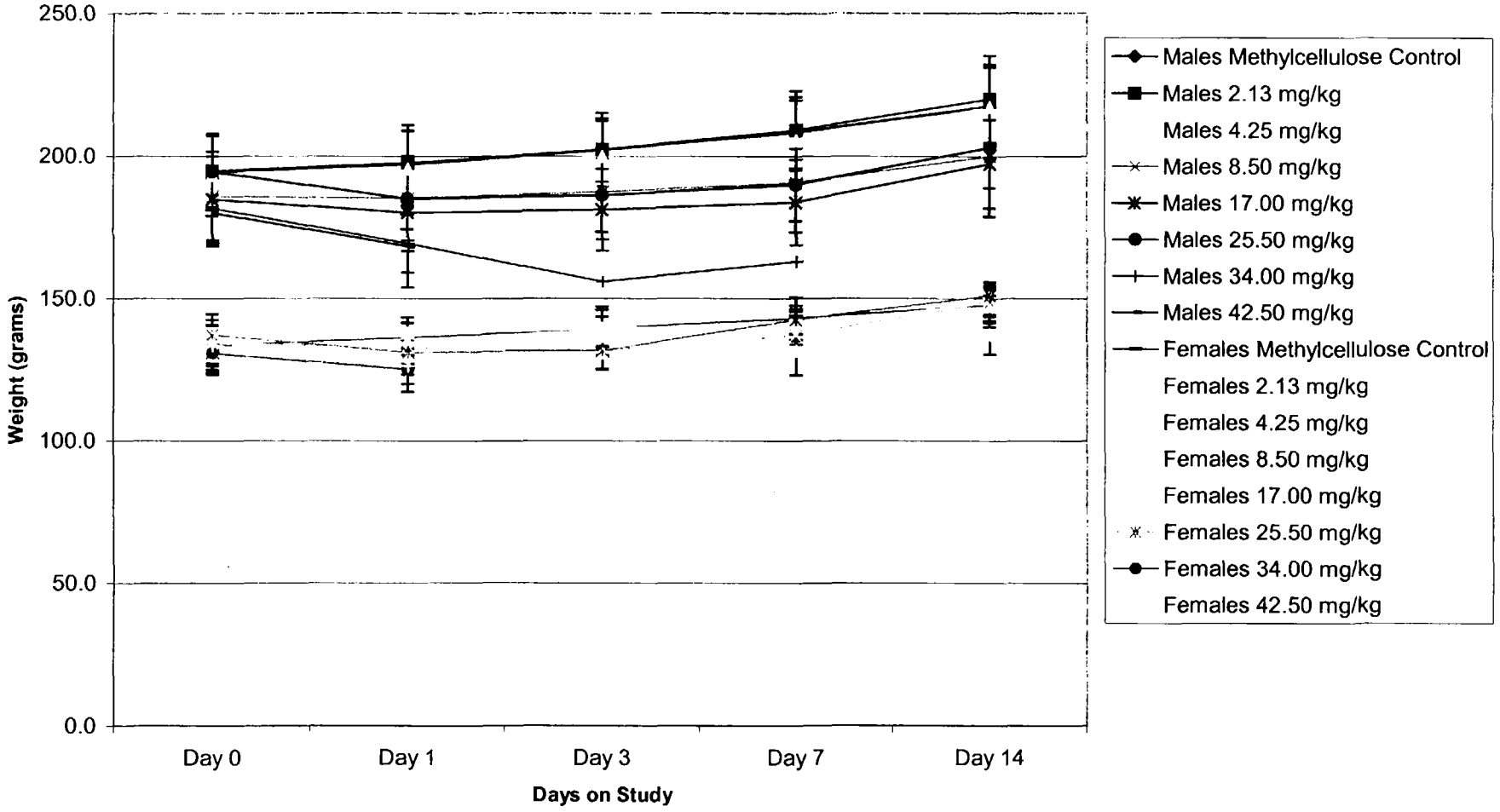


Table F-1
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Summary of Body Weights (grams)
Male Rats

Period		Methylcellulose Control	RDX in 1% Methylcellulose / 0.2% Tween 80 2.13 mg/kg	4.25 mg/kg	8.50 mg/kg	17.00 mg/kg	25.50 mg/kg	34.00 mg/kg	42.50 mg/kg
Day 0	Mean	194.5	194.7	193.3	186.0	184.8	194.5	181.8	180.2
	S.D.	12.68	12.69	14.24	15.57	15.12	13.41	12.45	11.86
	N	6	6	6	6	6	6	6	6
Day 1	Mean	197.0	197.5	195.5	185.2	180.2	185.0	169.3*	168.3*
	S.D.	12.07	13.43	13.31	14.74	13.54	10.79	10.21	14.45
	N	6	6	6	6	6	6	6	4
Day 3	Mean	202.2	202.3	200.0	187.5	181.2	186.3	156.0	(f)
	S.D.	11.16	12.88	12.51	16.67	14.34	12.90	0	
	N	6	6	6	6	5	3	1	
Day 7	Mean	208.3	209.0	205.7	190.7	183.8*	190.0	163.0*	(f)
	S.D.	12.52	13.91	13.89	17.42	15.01	12.77	0	
	N	6	6	6	6	5	3	1	
Day 14	Mean	217.5	220.0	217.2	200.0	197.3	203.0	(f)	(f)
	S.D.	13.66	15.21	14.91	21.27	15.59	14.14		
	N	6	6	6	6	4	2		

(f) = All animals died on study
* p less than or equal to 0.05
ANOVA with Holm-Sidak Method

Table F-2
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Summary of Body Weights (grams)
Female Rats

Period		Methylcellulose Control	RDX in 1% Methylcellulose / 0.2% Tween 80 2.13 mg/kg	4.25 mg/kg	8.50 mg/kg	17.00 mg/kg	25.50 mg/kg	34.00 mg/kg	42.50 mg/kg
Day 0	Mean	133.5	132.8	137.7	130.0	134.2	137.2	130.7	133.5
	S.D.	6.32	7.94	6.83	6.07	5.34	5.19	7.37	7.26
	N	6	6	6	6	6	6	6	6
Day 1	Mean	136.2	134.0	137.8	129.7	132.7	131.0	125.0*	126.2*
	S.D.	7.14	7.38	5.46	6.50	5.43	5.33	5.05	9.02
	N	6	6	6	6	6	6	5	6
Day 3	Mean	139.5	136.5	139.5	130.8	131.7	131.7	(f)	(f)
	S.D.	7.56	7.04	6.47	5.78	6.53	1.53		
	N	6	6	6	6	6	3		
Day 7	Mean	143.0	139.7	140.7	131.7	137.0	142.5	(f)	(f)
	S.D.	7.46	5.82	5.57	8.64	7.01	4.95		
	N	6	6	6	6	6	2		
Day 14	Mean	147.8	147.2	148.3	137.3*	148.7	151.0	(f)	(f)
	S.D.	7.91	5.81	6.22	6.98	5.01	0		
	N	6	6	6	6	6	1		

(f) = All animals died on study
* p less than or equal to 0.05
ANOVA with Holm-Sidak Method

Table F-3
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

14-Day Individual Body Weights (grams)
Male Rats

Group	Animal ID	Day 0	Day 1	Day 3	Day 7	Day 14
	04-185	206	208	212	224	242
Methylcellulose	04-186	176	182	191	195	202
Control	04-192	187	186	192	197	208
	04-194	198	198	200	205	217
	04-196	190	195	199	206	219
	04-221	210	213	219	223	217
	Mean	**194.5**	**197.0**	**202.2**	**208.3**	**217.5**
	SD	**12.68**	**12.07**	**11.16**	**12.52**	**13.66**
	04-177	185	186	193	198	210
2.13 mg/kg	04-187	207	214	217	224	235
	04-200	177	180	185	191	203
	04-209	192	195	199	206	213
	04-215	210	211	217	226	242
	04-217	197	199	203	209	217
	Mean	**194.7**	**197.5**	**202.3**	**209.0**	**220.0**
	SD	**12.69**	**13.43**	**12.88**	**13.91**	**15.21**
	04-181	205	203	208	213	228
4.25 mg/kg	04-183	186	185	189	196	209
	04-205	169	175	181	183	193
	04-208	208	212	214	222	235
	04-210	195	200	202	210	216
	04-220	197	198	206	210	222
	Mean	**193.3**	**195.5**	**200.0**	**205.7**	**217.2**
	SD	**14.24**	**13.31**	**12.51**	**13.89**	**14.91**
	04-173	191	192	195	197	213
8.50 mg/kg	04-174	169	170	169	171	173
	04-189	193	189	195	196	207
	04-190	200	195	198	207	215
	04-199	199	201	204	206	219
	04-212	164	164	164	167	173
	Mean	**186.0**	**185.2**	**187.5**	**190.7**	**200.0**
	SD	**15.57**	**14.74**	**16.67**	**17.42**	**21.27**
	04-179	213	205	206	208	214
17.00 mg/kg	04-193	170	167	169	170	195
	04-195	175	171	175	173	177
	04-201	182	179	178	186	203
	04-202	181	175	178	182	(f)
	04-204	188	184	(f)	(f)	(f)
	Mean	**184.8**	**180.2**	**181.2**	**183.8**	**197.3**
	SD	**15.12**	**13.54**	**14.34**	**15.01**	**15.59**
	04-178	196	189	190	193	213
25.50 mg/kg	04-180	192	184	(f)	(f)	(f)
	04-184	172	169	172	176	193
	04-207	206	192	(f)	(f)	(f)
	04-213	210	199	197	201	(f)
	04-219	191	177	(f)	(f)	(f)
	Mean	**194.5**	**185.0**	**186.3**	**190.0**	**203.0**
	SD	**13.41**	**10.79**	**12.90**	**12.77**	**14.14**
	04-175	182	168	(f)	(f)	(f)
34.00 mg/kg	04-182	201	188	(f)	(f)	(f)
	04-191	183	169	(f)	(f)	(f)
	04-198	188	169	(f)	(f)	(f)
	04-203	166	157	156	163	(f)
	04-206	171	165	(f)	(f)	(f)
	Mean	**181.8**	**169.3**	**156.0**	**163.0**	
	SD	**12.45**	**10.21**			
	04-172	183	(f)	(f)	(f)	(f)
42.50 mg/kg	04-176	182	172	(f)	(f)	(f)
	04-188	167	159	(f)	(f)	(f)
	04-211	169	155	(f)	(f)	(f)
	04-214	200	187	(f)	(f)	(f)
	04-216	180	(f)	(f)	(f)	(f)
	Mean	**180.2**	**168.3**			
	SD	**11.86**	**14.45**			

(f) = Animal died on study

Table F-4
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

14-Day Individual Body Weights (grams)
Female Rats

Group	Animal ID	Day 0	Day 1	Day 3	Day 7	Day 14
	04-249	134	134	138	143	146
Methylcellulose	04-253	126	126	131	133	138
Control	04-260	128	131	131	136	140
	04-262	143	142	146	148	154
	04-272	138	139	142	145	151
	04-273	132	145	149	153	158
	Mean	**133.5**	**136.2**	**139.5**	**143.0**	**147.8**
	SD	**6.32**	**7.14**	**7.56**	**7.46**	**7.91**
	04-237	134	135	137	144	149
2.13 mg/kg	04-241	135	135	137	138	149
	04-247	121	125	127	133	137
	04-274	142	144	145	148	153
	04-279	139	139	143	141	151
	04-281	126	126	130	134	144
	Mean	**132.8**	**134.0**	**136.5**	**139.7**	**147.2**
	SD	**7.94**	**7.38**	**7.04**	**5.82**	**5.81**
	04-239	137	135	138	136	146
4.25 mg/kg	04-243	126	130	128	133	138
	04-244	144	144	146	145	155
	04-268	145	144	145	148	154
	04-269	138	138	141	142	150
	04-271	136	136	139	140	147
	Mean	**137.7**	**137.8**	**139.5**	**140.7**	**148.3**
	SD	**6.83**	**5.46**	**6.47**	**5.57**	**6.22**
	04-233	126	124	128	128	132
8.50 mg/kg	04-234	136	136	134	141	146
	04-242	137	139	140	142	143
	04-246	125	127	131	130	138
	04-259	123	123	123	119	127
	04-263	133	129	129	130	138
	Mean	**130.0**	**129.7**	**130.8**	**131.7**	**137.3**
	SD	**6.07**	**6.50**	**5.78**	**8.64**	**6.98**
	04-238	133	130	129	140	152
17.00 mg/kg	04-248	132	128	127	131	143
	04-252	131	131	128	136	149
	04-256	129	128	126	127	142
	04-264	144	140	140	143	153
	04-275	136	139	140	145	153
	Mean	**134.2**	**132.7**	**131.7**	**137.0**	**148.7**
	SD	**5.34**	**5.43**	**6.53**	**7.01**	**5.01**
	04-240	138	131	(f)	(f)	(f)
25.50 mg/kg	04-261	128	124	(f)	(f)	(f)
	04-266	139	129	132	146	(f)
	04-270	143	140	133	139	151
	04-276	140	129	(f)	(f)	(f)
	04-280	135	133	130	(f)	(f)
	Mean	**137.2**	**131.0**	**131.7**	**142.5**	**151.0**
	SD	**5.19**	**5.33**	**1.53**	**4.95**	
	04-232	118	117	(f)	(f)	(f)
34.00 mg/kg	04-250	138	126	(f)	(f)	(f)
	04-251	127	(f)	(f)	(f)	(f)
	04-257	132	126	(f)	(f)	(f)
	04-258	132	125	(f)	(f)	(f)
	04-277	137	131	(f)	(f)	(f)
	Mean	**130.7**	**125.0**			
	SD	**7.37**	**5.05**			
	04-236	127	113	(f)	(f)	(f)
42.50 mg/kg	04-245	137	132	(f)	(f)	(f)
	04-254	135	129	(f)	(f)	(f)
	04-255	136	126	(f)	(f)	(f)
	04-265	123	119	(f)	(f)	(f)
	04-267	143	138	(f)	(f)	(f)
	Mean	**133.5**	**126.2**			
	SD	**7.26**	**9.02**			

(f) = Animal died on study

APPENDIX G

SUMMARY OF 14-DAY FOOD CONSUMPTION AND INDIVIDUAL FOOD CONSUMPTION DATA

Appendix G
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

14-Day Food Consumption

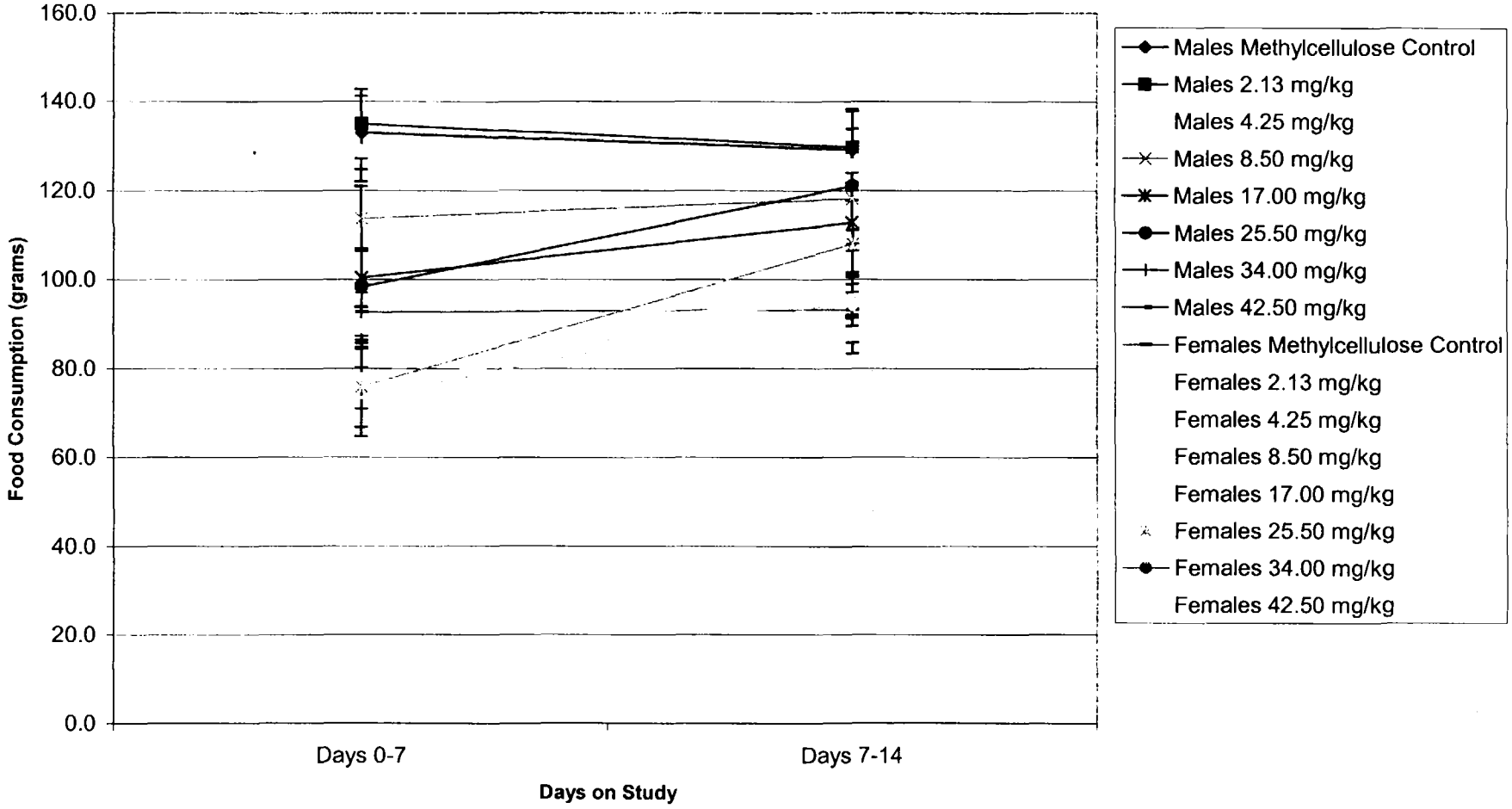


Table G-1
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Summary of Food Consumption (grams)
Male Rats

Period		Methylcellulose Control	RDX in 1% Methylcellulose / 0.2% Tween 80 2.13 mg/kg	4.25 mg/kg	8.50 mg/kg	17.00 mg/kg	25.50 mg/kg	34.00 mg/kg	42.50 mg/kg
Day 0-7	Mean	133.0	135.0	129.0	113.7*	100.4*	98.3*	97.0*	(f)
	S.D.	8.25	7.77	6.99	7.26	6.58	8.50	0	
	N	6	6	6	6	5	3	1	
Day 7-14	Mean	129.2	129.8	125.8	118.2	112.8	121.0	(f)	(f)
	S.D.	9.09	8.04	8.01	11.72	11.21	9.90		
	N	6	6	6	6	4	2		
Total	Mean	262.2	264.8	254.8	231.8	190.6	179.0	97.0	(f)
	S.D.	14.13	15.29	13.67	18.09	53.41	71.84	0	
	N	6	6	6	6	5	3	1	

(f) = All animals died on study
* p less than or equal to 0.05
ANOVA with Holm-Sidak Method

Table G-2
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Summary of Food Consumption (grams)
Female Rats

Period		Methylcellulose Control	RDX in 1% Methylcellulose / 0.2% Tween 80 2.13 mg/kg	4.25 mg/kg	8.50 mg/kg	17.00 mg/kg	25.50 mg/kg	34.00 mg/kg	42.50 mg/kg
Day 0-7	Mean	92.7	89.3	89.7	77.7*	73.5*	76.0*	(f)	(f)
	S.D.	6.31	4.55	4.03	6.71	6.66	11.31		
	N	6	6	6	6	6	2		
Day 7-14	Mean	93.2	94.2	95.3	87.7	95.3	108.0	(f)	(f)
	S.D.	7.36	2.93	3.61	4.37	5.75	0.00		
	N	6	6	6	6	6	1		
Total	Mean	185.8	183.5	185.0	165.3	168.8	130.0	(f)	(f)
	S.D.	13.60	7.01	7.18	10.60	11.94	65.05		
	N	6	6	6	6	6	2		

(f) = All animals died on study
* p less than or equal to 0.05
ANOVA with Holm-Sidak Method

Table G-3
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

14-Day Individual Food Consumption (grams)
Male Rats

Group	Animal ID	Days 0-7	Days 7-14	Total
	04-185	138	141	279
Methylcellulose	04-186	133	114	247
Control	04-192	125	126	251
	04-194	124	132	256
	04-196	132	128	260
	04-221	146	134	280
	Mean	**133.0**	**129.2**	**262.2**
	SD	**8.25**	**9.09**	**14.13**
	04-177	131	122	253
2.13 mg/kg	04-187	143	133	276
	04-200	124	121	245
	04-209	131	130	261
	04-215	144	143	287
	04-217	137	130	267
	Mean	**135.0**	**129.8**	**264.8**
	SD	**7.77**	**8.04**	**15.29**
	04-181	123	132	255
4.25 mg/kg	04-183	122	114	236
	04-205	124	118	242
	04-208	131	128	259
	04-210	136	129	265
	04-220	138	134	272
	Mean	**129.0**	**125.8**	**254.8**
	SD	**6.99**	**8.01**	**13.67**
	04-173	126	127	253
8.50 mg/kg	04-174	105	102	207
	04-189	111	116	227
	04-190	116	127	243
	04-199	115	130	245
	04-212	109	107	216
	Mean	**113.7**	**118.2**	**231.8**
	SD	**7.26**	**11.72**	**18.09**
	04-179	106	119	225
17.00 mg/kg	04-193	97	119	216
	04-195	92	96	188
	04-201	108	117	225
	04-202	99	(f)	99
	04-204	(f)	(f)	(f)
	Mean	**100.4**	**112.8**	**190.6**
	SD	**6.58**	**11.21**	**53.41**
	04-178	107	128	235
25.50 mg/kg	04-180	(f)	(f)	(f)
	04-184	90	114	204
	04-207	(f)	(f)	(f)
	04-213	98	(f)	98
	04-219	(f)	(f)	(f)
	Mean	**98.3**	**121.0**	**179.0**
	SD	**8.50**	**9.90**	**71.84**
	04-175	(f)	(f)	(f)
34.00 mg/kg	04-182	(f)	(f)	(f)
	04-191	(f)	(f)	(f)
	04-198	(f)	(f)	(f)
	04-203	97	(f)	97
	04-206	(f)	(f)	(f)
	Mean	**97.0**		**97.0**
	SD			
	04-172	(f)	(f)	(f)
42.50 mg/kg	04-176	(f)	(f)	(f)
	04-188	(f)	(f)	(f)
	04-211	(f)	(f)	(f)
	04-214	(f)	(f)	(f)
	04-216	(f)	(f)	(f)
	Mean			
	SD			

(f) = Animal died on study

Table G-4
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

14-Day Individual Food Consumption (grams)
Female Rats

Group	Animal ID	Day 0-7	Day 7-14	Total
	04-249	96	95	191
Methylcellulose	04-253	85	86	171
Control	04-260	86	84	170
	04-262	91	92	183
	04-272	98	99	197
	04-273	100	103	203
	Mean	**92.7**	**93.2**	**185.8**
	SD	**6.31**	**7.36**	**13.60**
	04-237	98	99	197
2.13 mg/kg	04-241	86	96	182
	04-247	90	93	183
	04-274	89	94	183
	04-279	86	92	178
	04-281	87	91	178
	Mean	**89.3**	**94.2**	**183.5**
	SD	**4.55**	**2.93**	**7.01**
	04-239	89	97	186
4.25 mg/kg	04-243	82	89	171
	04-244	92	93	185
	04-268	93	98	191
	04-269	92	97	189
	04-271	90	98	188
	Mean	**89.7**	**95.3**	**185.0**
	SD	**4.03**	**3.61**	**7.18**
	04-233	72	84	156
8.50 mg/kg	04-234	89	95	184
	04-242	80	85	165
	04-246	77	86	163
	04-259	78	91	169
	04-263	70	85	155
	Mean	**77.7**	**87.7**	**165.3**
	SD	**6.71**	**4.37**	**10.60**
	04-238	80	102	182
17.00 mg/kg	04-248	66	92	158
	04-252	70	93	163
	04-256	67	87	154
	04-264	77	101	178
	04-275	81	97	178
	Mean	**73.5**	**95.3**	**168.8**
	SD	**6.66**	**5.75**	**11.94**
	04-240	(f)	(f)	(f)
25.50 mg/kg	04-261	(f)	(f)	(f)
	04-266	84	(f)	84
	04-270	68	108	176
	04-276	(f)	(f)	(f)
	04-280	(f)	(f)	(f)
	Mean	**76.0**	**108.0**	**130.0**
	SD	**11.31**	**0.00**	**65.05**
	04-232	(f)	(f)	(f)
34.00 mg/kg	04-250	(f)	(f)	(f)
	04-251	(f)	(f)	(f)
	04-257	(f)	(f)	(f)
	04-258	(f)	(f)	(f)
	04-277	(f)	(f)	(f)
	Mean			
	SD			
	04-236	(f)	(f)	(f)
42.50 mg/kg	04-245	(f)	(f)	(f)
	04-254	(f)	(f)	(f)
	04-255	(f)	(f)	(f)
	04-265	(f)	(f)	(f)
	04-267	(f)	(f)	(f)
	Mean			
	SD			

(f) = Animal died on study

APPENDIX H

SUMMARY OF 14-DAY BODY WEIGHT GAINS AND INDIVIDUAL BODY WEIGHT GAIN DATA

Appendix H
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

14-Day Body Weight Gains

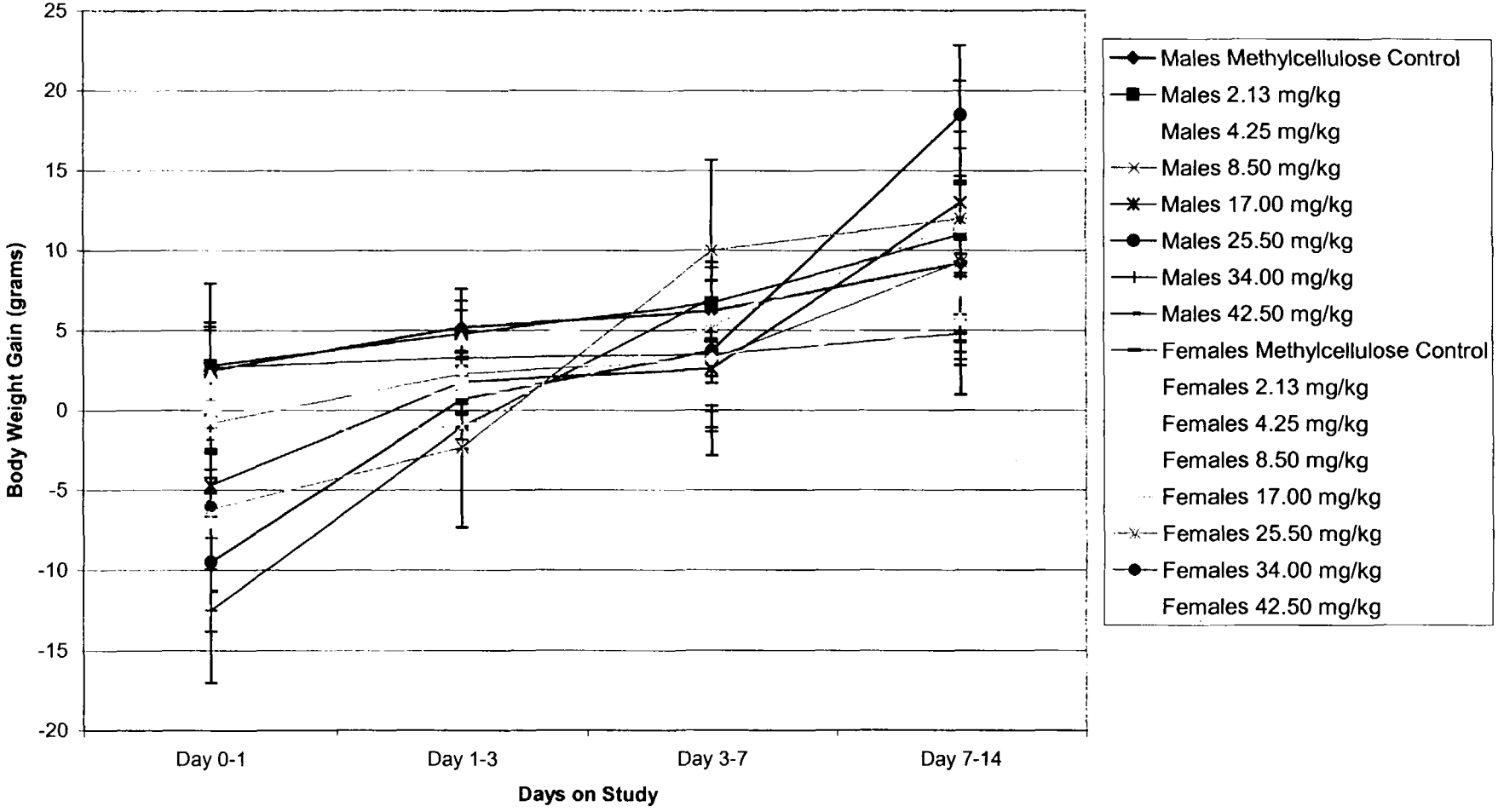


Table H-1
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Summary of Body Weight Gains (grams)
Male Rats

Period		Methylcellulose Control	RDX in 1% Methylcellulose / 0.2% Tween 80 2.13 mg/kg	4.25 mg/kg	8.50 mg/kg	17.00 mg/kg	25.50 mg/kg	34.00 mg/kg	42.50 mg/kg
Days 0-1	Mean	2.5	2.8	2.2	-0.8	-4.7*	-9.5*	-12.5*	-11.3*
	S.D.	2.74	2.23	3.31	2.93	1.97	4.32	4.51	2.75
	N	6	6	6	6	6	6	6	4
Days 1-3	Mean	5.2	4.8	4.5	2.3*	1.8*	0.7*	-1.0*	(f)
	S.D.	2.40	1.47	2.35	2.50	1.92	2.52	0	
	N	6	6	6	6	5	3	1	
Days 3-7	Mean	6.2	6.7	5.7	3.2	2.6	3.7	7.0	(f)
	S.D.	3.06	1.37	2.42	2.93	3.71	0.58	0	
	N	6	6	6	6	5	3	1	
Days 7-14	Mean	9.2	11.0	11.5	9.3	13.0	18.5	(f)	(f)
	S.D.	8.23	3.22	3.15	5.05	9.83	2.12		
	N	6	6	6	6	4	2		
Total	Mean	23.0	25.3	23.8	14.0	7.7*	-1.2*	-11.5*	-11.3*
	S.D.	9.90	4.46	2.04	6.72	12.13	15.87	5.89	2.75
	N	6	6	6	6	6	6	6	4

(f) = All animals died on study
* p less than or equal to 0.05
ANOVA with Holm-Sidak Method

Table H-2
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Summary of Body Weight Gains (grams)
Female Rats

Period		Methylcellulose Control	RDX in 1% Methylcellulose / 0.2% Tween 80 2.13 mg/kg	4.25 mg/kg	8.50 mg/kg	17.00 mg/kg	25.50 mg/kg	34.00 mg/kg	42.50 mg/kg
Days 0-1	Mean	2.7	1.2	0.2	-0.3	-1.5	-6.2*	-6.0*	-7.0*
	S.D.	5.24	1.60	2.04	2.34	2.74	3.76	3.91	3.88
	N	6	6	6	6	6	6	5	6
Days 1-3	Mean	3.3	2.5	1.7	1.2	-1.0*	-2.3	(f)	(f)
	S.D.	1.75	1.22	1.97	2.40	1.41	5.03		
	N	6	6	6	6	6	3		
Days 3-7	Mean	3.5	3.2	1.2	0.8	5.3	10.0	(f)	(f)
	S.D.	1.38	3.31	2.56	3.66	3.61	5.66		
	N	6	6	6	6	6	2		
Days 7-14	Mean	4.8	7.5	7.7	5.7	11.7*	12.0*	(f)	(f)
	S.D.	1.17	3.15	2.07	2.88	2.42	0		
	N	6	6	6	6	6	1		
Total	Mean	14.3	14.3	10.7	7.3*	14.5	-2.0*	-6.0*	-7.0*
	S.D.	5.75	2.58	1.37	3.44	4.09	7.75	3.91	3.88
	N	6	6	6	6	6	6	5	6

(f) = All animals died on study
* p less than or equal to 0.05
ANOVA with Holm-Sidak Method

Table H-3
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

14-Day Individual Body Weight Gains (grams)
Male Rats

Group	Animal ID	Day 0-1	Day 1-3	Day 3-7	Day 7-14	Total
	04-185	2	4	12	18	36
Methylcellulose	04-186	6	9	4	7	26
Control	04-192	-1	6	5	11	21
	04-194	0	2	5	12	19
	04-196	5	4	7	13	29
	04-221	3	6	4	-6	7
	Mean	**2.5**	**5.2**	**6.2**	**9.2**	**23.0**
	SD	**2.74**	**2.40**	**3.06**	**8.23**	**9.90**
	04-177	1	7	5	12	25
2.13 mg/kg	04-187	7	3	7	11	28
	04-200	3	5	6	12	26
	04-209	3	4	7	7	21
	04-215	1	6	9	16	32
	04-217	2	4	6	8	20
	Mean	**2.8**	**4.8**	**6.7**	**11.0**	**25.3**
	SD	**2.23**	**1.47**	**1.37**	**3.22**	**4.46**
	04-181	-2	5	5	15	23
4.25 mg/kg	04-183	-1	4	7	13	23
	04-205	6	6	2	10	24
	04-208	4	2	8	13	27
	04-210	5	2	8	6	21
	04-220	1	8	4	12	25
	Mean	**2.2**	**4.5**	**5.7**	**11.5**	**23.8**
	SD	**3.31**	**2.35**	**2.42**	**3.15**	**2.04**
	04-173	1	3	2	16	22
8.50 mg/kg	04-174	1	-1	2	2	4
	04-189	-4	6	1	11	14
	04-190	-5	3	9	8	15
	04-199	2	3	2	13	20
	04-212	0	0	3	6	9
	Mean	**-0.8**	**2.3**	**3.2**	**9.3**	**14.0**
	SD	**2.93**	**2.50**	**2.93**	**5.05**	**6.72**
	04-179	-8	1	2	6	1
17.00 mg/kg	04-193	-3	2	1	25	25
	04-195	-4	4	-2	4	2
	04-201	-3	-1	8	17	21
	04-202	-6	3	4	(f)	1
	04-204	-4	(f)	(f)	(f)	-4
	Mean	**-4.7**	**1.8**	**2.6**	**13.0**	**7.7**
	SD	**1.97**	**1.92**	**3.71**	**9.83**	**12.13**
	04-178	-7	1	3	20	17
25.50 mg/kg	04-180	-8	(f)	(f)	(f)	-8
	04-184	-3	3	4	17	21
	04-207	-14	(f)	(f)	(f)	-14
	04-213	-11	-2	4	(f)	-9
	04-219	-14	(f)	(f)	(f)	-14
	Mean	**-9.5**	**0.7**	**3.7**	**18.5**	**-1.2**
	SD	**4.32**	**2.52**	**0.58**	**2.12**	**15.87**
	04-175	-14	(f)	(f)	(f)	-14
34.00 mg/kg	04-182	-13	(f)	(f)	(f)	-13
	04-191	-14	(f)	(f)	(f)	-14
	04-198	-19	(f)	(f)	(f)	-19
	04-203	-9	-1	7	(f)	-3
	04-206	-6	(f)	(f)	(f)	-6
	Mean	**-12.5**	**-1.0**	**7.0**		**-11.5**
	SD	**4.51**				**5.89**
	04-172	(f)	(f)	(f)	(f)	(f)
42.50 mg/kg	04-176	-10	(f)	(f)	(f)	-10
	04-188	-8	(f)	(f)	(f)	-8
	04-211	-14	(f)	(f)	(f)	-14
	04-214	-13	(f)	(f)	(f)	-13
	04-216	(f)	(f)	(f)	(f)	(f)
	Mean	**-11.3**				**-11.3**
	SD	**2.75**				**2.75**

(f) = Animal died on study

Table H-4
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

14-Day Individual Body Weight Gains (grams)
Female Rats

Group	Animal ID	Day 0-1	Day 1-3	Day 3-7	Day 7-14	Total
	04-249	0	4	5	3	12
Methylcellulose	04-253	0	5	2	5	12
Control	04-260	3	0	5	4	12
	04-262	-1	4	2	6	11
	04-272	1	3	3	6	13
	04-273	13	4	4	5	26
	Mean	**2.7**	**3.3**	**3.5**	**4.8**	**14.3**
	SD	**5.24**	**1.75**	**1.38**	**1.17**	**5.75**
	04-237	1	2	7	5	15
2.13 mg/kg	04-241	0	2	1	11	14
	04-247	4	2	6	4	16
	04-274	2	1	3	5	11
	04-279	0	4	-2	10	12
	04-281	0	4	4	10	18
	Mean	**1.2**	**2.5**	**3.2**	**7.5**	**14.3**
	SD	**1.60**	**1.22**	**3.31**	**3.15**	**2.58**
	04-239	-2	3	-2	10	9
4.25 mg/kg	04-243	4	-2	5	5	12
	04-244	0	2	-1	10	11
	04-268	-1	1	3	6	9
	04-269	0	3	1	8	12
	04-271	0	3	1	7	11
	Mean	**0.2**	**1.7**	**1.2**	**7.7**	**10.7**
	SD	**2.04**	**1.97**	**2.56**	**2.07**	**1.37**
	04-233	-2	4	0	4	6
8.50 mg/kg	04-234	0	-2	7	5	10
	04-242	2	1	2	1	6
	04-246	2	4	-1	8	13
	04-259	0	0	-4	8	4
	04-263	-4	0	1	8	5
	Mean	**-0.3**	**1.2**	**0.8**	**5.7**	**7.3**
	SD	**2.34**	**2.40**	**3.66**	**2.88**	**3.44**
	04-238	-3	-1	11	12	19
17.00 mg/kg	04-248	-4	-1	4	12	11
	04-252	0	-3	8	13	18
	04-256	-1	-2	1	15	13
	04-264	-4	0	3	10	9
	04-275	3	1	5	8	17
	Mean	**-1.5**	**-1.0**	**5.3**	**11.7**	**14.5**
	SD	**2.74**	**1.41**	**3.61**	**2.42**	**4.09**
	04-240	-7	(f)	(f)	(f)	-7
25.50 mg/kg	04-261	-4	(f)	(f)	(f)	-4
	04-266	-10	3	14	(f)	7
	04-270	-3	-7	6	12	8
	04-276	-11	(f)	(f)	(f)	-11
	04-280	-2	-3	(f)	(f)	-5
	Mean	**-6.2**	**-2.3**	**10.0**	**12.0**	**-2.0**
	SD	**3.76**	**5.03**	**5.66**		**7.75**
	04-232	-1	(f)	(f)	(f)	-1
34.00 mg/kg	04-250	-12	(f)	(f)	(f)	-12
	04-251	(f)	(f)	(f)	(f)	(f)
	04-257	-6	(f)	(f)	(f)	-6
	04-258	-7	(f)	(f)	(f)	-7
	04-277	-6	(f)	(f)	(f)	-6
	Mean	**-6.4**				**-6**
	SD	**3.91**				**3.91**
	04-236	-14	(f)	(f)	(f)	-14
42.50 mg/kg	04-245	-5	(f)	(f)	(f)	-5
	04-254	-6	(f)	(f)	(f)	-6
	04-255	-10	(f)	(f)	(f)	-10
	04-265	-4	(f)	(f)	(f)	-4
	04-267	-5	(f)	(f)	(f)	-5
	Mean	**-7.3**				**-7.3**
	SD	**3.88**				**3.88**

(f) = Animal died on study

APPENDIX I

SUMMARY OF 14-DAY ORGAN WEIGHTS AND INDIVIDUAL ORGAN WEIGHT DATA

Table I-1
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Summary of 14-Day Organ Weights
Male Rats

Absolute Organ Weight (grams)

		Methylcellulose	RDX in 1% Methylcellulose / 0.2% Tween 80						
		Control	2.13 mg/kg	4.25 mg/kg	8.50 mg/kg	17.00 mg/kg	25.50 mg/kg	34.00 mg/kg	42.50 mg/kg
Body Weight	Mean	221.8	220.2	218.3	203.0	199.0	205.5	(f)	(f)
	S.D.	18.34	14.96	14.77	21.53	16.79	10.61		
	N	5	6	6	6	4	2		
Adrenals	Mean	0.0460	0.0455	0.0458	0.0497	0.0460	0.0450	(f)	(f)
	S.D.	0.00498	0.01214	0.00571	0.00802	0.00216	0.00707		
	N	6	6	6	6	4	2		
Brain	Mean	1.8283	1.7712	1.8217	1.8067	1.8000	1.8205	(f)	(f)
	S.D.	0.03920	0.04025	0.01329	0.06713	0.08756	0.04172		
	N	6	6	6	6	4	2		
Heart	Mean	0.7293	0.7147	0.7267	0.6685	0.6500	0.7375	(f)	(f)
	S.D.	0.09182	0.06895	0.02805	0.04764	0.06055	0.08132		
	N	6	6	6	6	4	2		
Kidneys	Mean	1.8017	1.6233	1.6350	1.5867	1.5600	1.5475	(f)	(f)
	S.D.	0.23112	0.11978	0.10426	0.14665	0.14900	0.10253		
	N	6	6	6	6	4	2		
Liver	Mean	9.6050	9.2810	9.4733	8.7350	8.5925	9.9525	(f)	(f)
	S.D.	1.18553	0.96603	0.97596	1.27995	1.15667	1.46725		
	N	6	6	6	6	4	2		
Spleen	Mean	0.4962	0.5058	0.5048	0.4717	0.4750	0.5055	(f)	(f)
	S.D.	0.05389	0.03314	0.03505	0.04956	0.04123	0.00778		
	N	6	6	6	6	4	2		
Testes	Mean	2.7100	2.6752	2.7783	2.6383	2.4600	2.3290	(f)	(f)
	S.D.	0.27232	0.20671	0.08931	0.25380	0.38497	0.15415		
	N	6	6	6	6	4	2		
Thymus	Mean	0.3577	0.3823	0.3628	0.3568	0.3783	0.3625	(f)	(f)
	S.D.	0.02778	0.01093	0.04044	0.07811	0.04739	0.02192		
	N	6	6	6	6	4	2		
Epididymides	Mean	0.5443	0.5297	0.5732	0.4933	0.4325	0.4200	(f)	(f)
	S.D.	0.09151	0.10393	0.03313	0.08008	0.11529	0.06505		
	N	6	6	6	6	4	2		

(f) = All animals died on study

Table I-2
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Summary of 14-Day Organ Weights
Female Rats

Absolute Organ Weight (grams)

		Methylcellulose Control	RDX in 1% Methylcellulose / 0.2% Tween 80						
			2.13 mg/kg	4.25 mg/kg	8.50 mg/kg	17.00 mg/kg	25.50 mg/kg	34.00 mg/kg	42.50 mg/kg
Body Weight	Mean	147.3	146.8	148.8	137.8	151.2	151.0	(f)	(f)
	S.D.	7.55	6.55	6.18	6.43	6.43	0		
	N	6	6	6	6	6	1		
Adrenals	Mean	0.0612	0.0522	0.0554	0.0537	0.0523	0.0680	(f)	(f)
	S.D.	0.00749	0.00578	0.01099	0.00653	0.00554	0		
	N	6	6	5	6	6	1		
Brain	Mean	1.6552	1.6437	1.6750	1.6592	1.6808	1.6530	(f)	(f)
	S.D.	0.06259	0.09125	0.03482	0.07893	0.03218	0		
	N	6	6	6	6	6	1		
Heart	Mean	0.5746	0.5653	0.6065	0.5148	0.5598	0.6130	(f)	(f)
	S.D.	0.05584	0.04607	0.03811	0.05226	0.05853	0		
	N	5	6	6	6	6	1		
Kidneys	Mean	1.1803	1.1802	1.1933	1.1277	1.2232	1.2270	(f)	(f)
	S.D.	0.08107	0.08844	0.06049	0.04550	0.05364	0		
	N	6	6	6	6	6	1		
Liver	Mean	5.7798	5.8357	5.7638	5.0757*	5.8698	5.7410	(f)	(f)
	S.D.	0.60971	0.24449	0.39722	0.39582	0.34759	0		
	N	6	6	6	6	6	1		
Ovaries	Mean	0.1098	0.1018	0.1087	0.0872	0.1022	0.0640	(f)	(f)
	S.D.	0.02217	0.01032	0.01457	0.01755	0.02145	0		
	N	6	6	6	6	6	1		
Spleen	Mean	0.3828	0.3943	0.4083	0.3483	0.4258	0.3600	(f)	(f)
	S.D.	0.03224	0.0236	0.02238	0.02347	0.03639	0		
	N	6	6	6	6	6	1		
Thymus	Mean	0.3398	0.3613	0.3327	0.3012	0.2937	0.2430	(f)	(f)
	S.D.	0.03161	0.03785	0.04008	0.03102	0.05415	0		
	N	6	6	6	6	6	1		
Uterus	Mean	0.3110	0.3623	0.2843	0.2195	0.1935	0.3430	(f)	(f)
	S.D.	0.11838	0.09562	0.0413	0.08435	0.03774	0		
	N	6	6	6	6	6	1		

(f) = All animals died on study
* p less than or equal to 0.05
ANOVA with Holm-Sidak Method

Table I-3
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Summary of 14-Day Organ Weights
Male Rats

% Body Weight

		Methylcellulose Control	RDX in 1% Methylcellulose / 0.2% Tween 80						
			2.13 mg/kg	4.25 mg/kg	8.50 mg/kg	17.00 mg/kg	25.50 mg/kg	34.00 mg/kg	42.50 mg/kg
Adrenals	Mean	0.0209	0.0206	0.0211	0.0243	0.0232	0.0218	(f)	(f)
	S.D.	0.00254	0.00508	0.00359	0.00180	0.00130	0.00231		
	N	5	6	6	6	4	2		
Brain	Mean	0.8257	0.8073	0.8377	0.8965	0.9102	0.8865	(f)	(f)
	S.D.	0.05045	0.05321	0.05981	0.07735	0.09692	0.02546		
	N	5	6	6	6	4	2		
Heart	Mean	0.3337	0.3244	0.3336	0.3306	0.3265	0.3604	(f)	(f)
	S.D.	0.03281	0.01785	0.01707	0.01764	0.00883	0.05817		
	N	5	6	6	6	4	2		
Kidneys	Mean	0.8211	0.7373	0.7497	0.7829	0.7843	0.7528	(f)	(f)
	S.D.	0.13053	0.02156	0.03272	0.02967	0.04021	0.01104		
	N	5	6	6	6	4	2		
Liver	Mean	4.3527	4.2073	4.3307	4.2873	4.3062	4.8311	(f)	(f)
	S.D.	0.25212	0.17459	0.19411	0.20242	0.30241	0.46464		
	N	5	6	6	6	4	2		
Spleen	Mean	0.2259	0.2299	0.2312	0.2327	0.2390	0.2464	(f)	(f)
	S.D.	0.01542	0.0082	0.00481	0.01227	0.01383	0.01650		
	N	5	6	6	6	4	2		
Testes	Mean	1.2087	1.2155	1.2760	1.3019	1.2312	1.1368	(f)	(f)
	S.D.	0.05420	0.06110	0.06716	0.06099	0.10859	0.13369		
	N	5	6	6	6	4	2		
Thymus	Mean	0.1646	0.1742	0.1665	0.1745	0.1912	0.1764	(f)	(f)
	S.D.	0.01955	0.01101	0.01861	0.02610	0.02800	0.00156		
	N	5	6	6	6	4	2		
Epididymides	Mean	0.2436	0.2393	0.2628	0.2425	0.2150	0.2055	(f)	(f)
	S.D.	0.02656	0.03525	0.01005	0.02898	0.04353	0.04226		
	N	5	6	6	6	4	2		

(f) = All animals died on study

Table I-4
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Summary of 14-Day Organ Weights
Female Rats

% Body Weight

		Methylcellulose	RDX in 1% Methylcellulose / 0.2% Tween 80						
		Control	2.13 mg/kg	4.25 mg/kg	8.50 mg/kg	17.00 mg/kg	25.50 mg/kg	34.00 mg/kg	42.50 mg/kg
Adrenals	Mean	0.0415	0.0356	0.0375	0.0391	0.0347	0.0450	(f)	(f)
	S.D.	0.00452	0.00456	0.00758	0.00599	0.00356	0		
	N	6	6	5	6	6	1		
Brain	Mean	1.1257	1.1197	1.1268	1.2050	1.1132	1.0947	(f)	(f)
	S.D.	0.06781	0.04636	0.04565	0.06076	0.04039	0		
	N	6	6	6	6	6	1		
Heart	Mean	0.3889	0.3852	0.4073	0.3730	0.3702	0.4060	(f)	(f)
	S.D.	0.02414	0.03020	0.01372	0.02556	0.03382	0		
	N	5	6	6	6	6	1		
Kidneys	Mean	0.8007	0.8031	0.8018	0.8188	0.8096	0.8126	(f)	(f)
	S.D.	0.02377	0.03593	0.02382	0.03083	0.03038	0		
	N	6	6	6	6	6	1		
Liver	Mean	3.9146	3.9758	3.8695	3.6806	3.8832	3.8020	(f)	(f)
	S.D.	0.23811	0.09649	0.12670	0.18754	0.17083	0		
	N	6	6	6	6	6	1		
Ovaries	Mean	0.0742	0.0695	0.0730	0.0631	0.0673	0.0424	(f)	(f)
	S.D.	0.01222	0.00808	0.00943	0.01204	0.01216	0		
	N	6	6	6	6	6	1		
Spleen	Mean	0.2599	0.2691	0.2747	0.2527	0.2814	0.2384	(f)	(f)
	S.D.	0.01749	0.02083	0.01696	0.01213	0.01594	0		
	N	6	6	6	6	6	1		
Thymus	Mean	0.2313	0.2463	0.2243	0.2183	0.1942	0.1609	(f)	(f)
	S.D.	0.02552	0.02598	0.03209	0.01733	0.03449	0		
	N	6	6	6	6	6	1		
Uterus	Mean	0.2091	0.2463	0.1908	0.1604	0.1280	0.2272	(f)	(f)
	S.D.	0.07399	0.06162	0.02474	0.06664	0.02324	0		
	N	6	6	6	6	6	1		

(f) = All animals died on study

Table I-5
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Summary of 14-Day Organ Weights
Male Rats

% Brain Weight

		Methylcellulose Control	RDX in 1% Methylcellulose / 0.2% Tween 80						
			2.13 mg/kg	4.25 mg/kg	8.50 mg/kg	17.00 mg/kg	25.50 mg/kg	34.00 mg/kg	42.50 mg/kg
Adrenals	Mean	2.5151	2.5667	2.5166	2.7418	2.5585	2.4680	(f)	(f)
	S.D.	0.25238	0.67215	0.31761	0.38284	0.13874	0.33185		
	N	6	6	6	6	4	2		
Heart	Mean	39.8514	40.3770	39.8964	36.9966	36.1741	40.5727	(f)	(f)
	S.D.	4.55729	4.15899	1.70507	2.16314	3.81209	5.39653		
	N	6	6	6	6	4	2		
Kidneys	Mean	98.5859	91.6534	89.7428	87.7657	87.0556	84.9619	(f)	(f)
	S.D.	13.05725	6.37499	5.45899	6.82484	12.26434	3.68498		
	N	6	6	6	6	4	2		
Liver	Mean	524.6300	524.0266	520.0021	482.3762	477.8826	545.9103	(f)	(f)
	S.D.	55.95312	53.28353	53.04503	59.37304	65.50349	68.08550		
	N	6	6	6	6	4	2		
Spleen	Mean	27.1155	28.5654	27.7102	26.0979	26.4024	27.7793	(f)	(f)
	S.D.	2.62453	1.85497	1.86579	2.49273	2.09678	1.06386		
	N	6	6	6	6	4	2		
Testes	Mean	148.0885	150.9745	152.5012	145.9182	137.2304	128.0625	(f)	(f)
	S.D.	12.78060	10.25013	4.14018	11.65767	25.64887	11.40215		
	N	6	6	6	6	4	2		
Thymus	Mean	19.5813	21.5940	19.9190	19.7037	20.9557	19.9035	(f)	(f)
	S.D.	1.75805	0.72392	2.22084	3.99236	1.66396	0.74796		
	N	6	6	6	6	4	2		
Epididymides	Mean	29.7100	29.8408	31.4621	27.2348	24.1747	23.1176	(f)	(f)
	S.D.	4.47555	5.46076	1.75984	3.89737	7.23640	4.10318		
	N	6	6	6	6	4	2		

(f) = All animals died on study

Table I-6
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Summary of 14-Day Organ Weights
Female Rats

% Brain Weight

		Methylcellulose	RDX in 1% Methylcellulose / 0.2% Tween 80						
		Control	2.13 mg/kg	4.25 mg/kg	8.50 mg/kg	17.00 mg/kg	25.50 mg/kg	34.00 mg/kg	42.50 mg/kg
Adrenals	Mean	3.7049	3.1842	2.7765	3.2374	3.1112	4.1137	(f)	(f)
	S.D.	0.52141	0.43197	1.50125	0.38617	0.29197	0		
	N	6	6	5	6	6	1		
Heart	Mean	29.2123	34.4501	36.2061	31.0333	33.3042	37.0841	(f)	(f)
	S.D.	14.69954	2.98832	2.07593	2.76871	3.40265	0		
	N	5	6	6	6	6	1		
Kidneys	Mean	71.3772	71.7753	71.2220	68.0848	72.7446	74.2287	(f)	(f)
	S.D.	5.30405	3.14935	2.65208	4.03623	1.86797	0		
	N	6	6	6	6	6	1		
Liver	Mean	349.5126	355.7331	344.0422	306.5136*	349.0536	347.3079	(f)	(f)
	S.D.	38.31430	20.23026	21.30010	27.80169	15.63812	0		
	N	6	6	6	6	6	1		
Ovaries	Mean	6.6390	6.2274	6.4902	5.2772	6.0644	3.8717	(f)	(f)
	S.D.	1.34039	0.83337	0.87159	1.14324	1.17441	0		
	N	6	6	6	6	6	1		
Spleen	Mean	23.1568	24.0929	24.3939	21.0277	25.3328	21.7786	(f)	(f)
	S.D.	2.17579	2.45645	1.57289	1.60782	2.08320	0		
	N	6	6	6	6	6	1		
Thymus	Mean	20.5263	22.0150	19.8990	18.1905	17.5066	14.7005	(f)	(f)
	S.D.	1.65818	2.35438	2.72328	2.06319	3.38623	0		
	N	6	6	6	6	6	1		
Uterus	Mean	18.8829	22.0489	16.9814	13.3605	11.4976	20.7502	(f)	(f)
	S.D.	7.56167	5.81775	2.47147	5.62926	2.10692	0		
	N	6	6	6	6	6	1		

(f) = All animals died on study
* p less than or equal to 0.05
ANOVA with Holm-Sidak Method

Table I-7
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

14-Day Individual Organ Weights (grams)
Male Rats

Group	Animal ID	Body Weight	Adrenals	Brain	Heart	Kidneys	Liver	Spleen	Testes	Thymus	Epididymides
	04-185	242	0.040	1.850	0.850	1.850	10.720	0.590	3.100	0.383	0.630
Methylcellulose	04-186	202	0.045	1.770	0.650	1.590	8.520	0.440	2.440	0.400	0.450
Control	04-192	208	0.044	1.790	0.640	2.180	8.710	0.460	2.540	0.340	0.480
	04-194	217	0.047	1.840	0.830	1.550	9.040	0.520	2.450	0.338	0.482
	04-196		0.045	1.850	0.673	1.740	9.210	0.470	2.840	0.331	0.547
	04-221	240	0.055	1.870	0.733	1.900	11.430	0.497	2.890	0.354	0.677
	Mean	**221.8**	**0.0460**	**1.8283**	**0.7293**	**1.8017**	**9.6050**	**0.4962**	**2.7100**	**0.3577**	**0.5443**
	SD	**18.34**	**0.00498**	**0.03920**	**0.09182**	**0.23112**	**1.18553**	**0.05389**	**0.27232**	**0.02778**	**0.09151**
	04-177	210	0.045	1.710	0.680	1.540	8.686	0.497	2.321	0.371	0.380
2.13 mg/kg	04-187	235	0.051	1.740	0.840	1.690	10.250	0.530	2.860	0.390	0.590
	04-200	203	0.047	1.790	0.660	1.440	7.950	0.490	2.580	0.370	0.480
	04-209	212	0.022	1.767	0.658	1.620	8.800	0.466	2.680	0.394	0.468
	04-215	241	0.056	1.810	0.740	1.780	10.410	0.559	2.880	0.377	0.658
	04-217	220	0.052	1.810	0.710	1.670	9.590	0.493	2.730	0.392	0.602
	Mean	**220.2**	**0.0455**	**1.7712**	**0.7147**	**1.6233**	**9.2810**	**0.5058**	**2.6752**	**0.3823**	**0.5297**
	SD	**14.96**	**0.01214**	**0.04025**	**0.06895**	**0.11978**	**0.96603**	**0.03314**	**0.20671**	**0.01093**	**0.10393**
	04-181	228	0.043	1.800	0.770	1.660	9.730	0.520	2.730	0.370	0.590
4.25 mg/kg	04-183	209	0.044	1.820	0.710	1.540	8.930	0.480	2.740	0.370	0.540
	04-205	193	0.052	1.820	0.700	1.540	7.770	0.450	2.680	0.320	0.540
	04-208	232	0.041	1.840	0.740	1.820	10.130	0.550	2.940	0.330	0.627
	04-210	221	0.041	1.830	0.700	1.600	9.840	0.520	2.790	0.434	0.564
	04-220	227	0.054	1.820	0.740	1.650	10.440	0.509	2.790	0.353	0.578
	Mean	**218.3**	**0.0458**	**1.8217**	**0.7267**	**1.6350**	**9.4733**	**0.5048**	**2.7783**	**0.3628**	**0.5732**
	SD	**14.77**	**0.00571**	**0.01329**	**0.02805**	**0.10426**	**0.97596**	**0.03505**	**0.08931**	**0.04044**	**0.03313**
	04-173	213	0.054	1.760	0.690	1.720	9.490	0.530	2.740	0.400	0.510
8.50 mg/kg	04-174	173	0.036	1.720	0.630	1.340	6.850	0.420	2.210	0.300	0.334
	04-189	207	0.053	1.810	0.690	1.640	8.660	0.480	2.840	0.410	0.520
	04-190	220	0.054	1.850	0.701	1.650	9.770	0.470	2.860	0.356	0.556
	04-199	225	0.057	1.910	0.710	1.690	10.040	0.520	2.720	0.442	0.533
	04-212	180	0.044	1.790	0.590	1.480	7.600	0.410	2.460	0.233	0.507
	Mean	**203.0**	**0.0497**	**1.8067**	**0.6685**	**1.5867**	**8.7350**	**0.4717**	**2.6383**	**0.3568**	**0.4933**
	SD	**21.53**	**0.00802**	**0.06713**	**0.04764**	**0.14665**	**1.27995**	**0.04956**	**0.25380**	**0.07811**	**0.08008**
	04-179	214	0.046	1.680	0.680	1.770	9.000	0.470	2.870	0.320	0.560
17.00 mg/kg	04-193	195	0.047	1.860	0.640	1.510	8.770	0.470	2.520	0.410	0.450
	04-195	177	0.043	1.790	0.570	1.420	6.950	0.430	1.940	0.360	0.280
	04-201	210	0.048	1.870	0.710	1.540	9.650	0.530	2.510	0.423	0.44
	04-202	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-204	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	Mean	**199.0**	**0.0460**	**1.8000**	**0.6500**	**1.5600**	**8.5925**	**0.4750**	**2.4600**	**0.3783**	**0.4325**
	SD	**16.79**	**0.00216**	**0.08756**	**0.06055**	**0.14900**	**1.15667**	**0.04123**	**0.38497**	**0.04739**	**0.11529**
	04-178	213	0.050	1.850	0.680	1.620	10.990	0.500	2.220	0.378	0.374
25.50 mg/kg	04-180	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-184	198	0.040	1.791	0.795	1.475	8.915	0.511	2.438	0.347	0.466
	04-207	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-213	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-219	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	Mean	**205.5**	**0.0450**	**1.8205**	**0.7375**	**1.5475**	**9.9525**	**0.5055**	**2.3290**	**0.3625**	**0.4200**
	SD	**10.61**	**0.00707**	**0.04172**	**0.08132**	**0.10253**	**1.46725**	**0.00778**	**0.15415**	**0.02192**	**0.06505**
	04-175	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
34.00 mg/kg	04-182	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-191	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-198	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-203	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-206	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	Mean										
	SD										
	04-172	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
42.50 mg/kg	04-176	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-188	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-211	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-214	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-216	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	Mean										
	SD										

= No data
(f) = Animal died on study

Table I-8
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

14-Day Individual Organ Weights (grams)
Female Rats

Group	Animal ID	Body Weight	Adrenals	Brain	Heart	Kidneys	Liver	Ovaries	Spleen	Thymus	Uterus
	04-249	146	0.052	1.725		1.202	5.848	0.113	0.384	0.380	0.257
Methylcellulose	04-253	138	0.054	1.581	0.509	1.069	4.939	0.089	0.349	0.300	0.185
Control	04-260	140	0.062	1.712	0.527	1.092	5.135	0.088	0.363	0.361	0.211
	04-262	150	0.068	1.601	0.645	1.252	6.052	0.135	0.437	0.354	0.502
	04-272	152	0.071	1.617	0.592	1.207	6.378	0.097	0.363	0.338	0.376
	04-273	158	0.060	1.695	0.600	1.260	6.327	0.137	0.401	0.306	0.335
	Mean	**147.3**	**0.0612**	**1.6552**	**0.5746**	**1.1803**	**5.7798**	**0.1098**	**0.3828**	**0.3398**	**0.3110**
	SD	**7.55**	**0.00749**	**0.06259**	**0.05584**	**0.08107**	**0.60971**	**0.02217**	**0.03224**	**0.03161**	**0.11838**
	04-237	149	0.055	1.786	0.613	1.250	5.725	0.083	0.364	0.371	0.401
2.13 mg/kg	04-241	149	0.047	1.608	0.601	1.189	6.049	0.100	0.436	0.393	0.527
	04-247	137	0.060	1.508	0.572	1.032	5.539	0.104	0.400	0.331	0.298
	04-274	156	0.056	1.681	0.589	1.230	6.206	0.110	0.388	0.374	0.312
	04-279	148	0.050	1.651	0.510	1.259	5.733	0.102	0.389	0.301	0.375
	04-281	142	0.045	1.628	0.507	1.121	5.762	0.112	0.389	0.398	0.261
	Mean	**146.8**	**0.0522**	**1.6437**	**0.5653**	**1.1802**	**5.8357**	**0.1018**	**0.3943**	**0.3613**	**0.3623**
	SD	**6.55**	**0.00578**	**0.09125**	**0.04607**	**0.08844**	**0.24449**	**0.01032**	**0.02360**	**0.03785**	**0.09562**
	04-239	146	0.070	1.639	0.583	1.125	5.364	0.115	0.387	0.351	0.308
4.25 mg/kg	04-243	138	0.046	1.679	0.553	1.142	5.212	0.098	0.401	0.343	0.227
	04-244	155	0.043	1.702	0.640	1.281	6.259	0.097	0.413	0.264	0.268
	04-268	153		1.714	0.607	1.243	5.982	0.133	0.382	0.332	0.346
	04-269	152	0.058	1.689	0.658	1.203	5.924	0.096	0.431	0.321	0.262
	04-271	149	0.060	1.627	0.598	1.166	5.842	0.113	0.436	0.385	0.295
	Mean	**148.8**	**0.0554**	**1.6750**	**0.6065**	**1.1933**	**5.7638**	**0.1087**	**0.4083**	**0.3327**	**0.2843**
	SD	**6.18**	**0.01099**	**0.03482**	**0.03811**	**0.06049**	**0.39722**	**0.01457**	**0.02238**	**0.04008**	**0.04130**
	04-233	132	0.063	1.720	0.450	1.072	4.524	0.055	0.314	0.247	0.168
8.50 mg/kg	04-234	146	0.044	1.657	0.564	1.192	5.710	0.086	0.373	0.338	0.191
	04-242	143	0.050	1.729	0.561	1.155	5.276	0.103	0.374	0.314	0.283
	04-246	138	0.056	1.590	0.476	1.080	4.903	0.103	0.331	0.291	0.168
	04-259	129	0.052	1.540	0.478	1.130	5.003	0.089	0.347	0.300	0.361
	04-263	139	0.057	1.719	0.560	1.137	5.038	0.087	0.351	0.317	0.146
	Mean	**137.8**	**0.0537**	**1.6592**	**0.5148**	**1.1277**	**5.0757**	**0.0872**	**0.3483**	**0.3012**	**0.2195**
	SD	**6.43**	**0.00653**	**0.07893**	**0.05226**	**0.04550**	**0.39582**	**0.01755**	**0.02347**	**0.03102**	**0.08435**
	04-238	152	0.052	1.662	0.647	1.207	5.988	0.103	0.466	0.347	0.190
17.00 mg/kg	04-248	143	0.050	1.645	0.505	1.170	5.459	0.087	0.392	0.305	0.195
	04-252	149	0.053	1.719	0.526	1.277	6.230	0.105	0.398	0.193	0.182
	04-256	146	0.052	1.662	0.535	1.169	5.429	0.079	0.391	0.286	0.174
	04-264	158	0.062	1.722	0.620	1.297	6.174	0.141	0.466	0.299	0.265
	04-275	159	0.045	1.675	0.526	1.219	5.939	0.098	0.442	0.332	0.155
	Mean	**151.2**	**0.0523**	**1.6808**	**0.5598**	**1.2232**	**5.8698**	**0.1022**	**0.4258**	**0.2937**	**0.1935**
	SD	**6.43**	**0.00554**	**0.03218**	**0.05853**	**0.05364**	**0.34759**	**0.02145**	**0.03639**	**0.05415**	**0.03774**
	04-240	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
25.50 mg/kg	04-261	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-266	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-270	151	0.068	1.653	0.613	1.227	5.741	0.064	0.360	0.243	0.343
	04-276	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-280	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	Mean	**151.0**	**0.0680**	**1.6530**	**0.6130**	**1.2270**	**5.7410**	**0.0640**	**0.3600**	**0.2430**	**0.3430**
	SD	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
	04-232	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
34.00 mg/kg	04-250	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-251	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-257	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-258	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-277	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	Mean										
	SD										
	04-236	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
42.50 mg/kg	04-245	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-254	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-255	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-265	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-267	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	Mean										
	SD										

= No data
(f) = Animal died on study

Table I-9
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

14-Day Individual Organ Weights (grams)
Male Rats

% Body Weight

Group	Animal ID	Adrenals	Brain	Heart	Kidneys	Liver	Spleen	Testes	Thymus	Epididymides
	04-185	0.017	0.764	0.351	0.764	4.430	0.244	1.281	0.158	0.260
Methylcellulose	04-186	0.022	0.876	0.322	0.787	4.218	0.218	1.208	0.198	0.223
Control	04-192	0.021	0.861	0.308	1.048	4.188	0.221	1.221	0.163	0.231
	04-194	0.022	0.848	0.382	0.714	4.166	0.240	1.129	0.156	0.222
	04-196									
	04-221	0.023	0.779	0.305	0.792	4.763	0.207	1.204	0.148	0.282
	Mean	**0.0209**	**0.8257**	**0.3337**	**0.8211**	**4.3527**	**0.2259**	**1.2087**	**0.1646**	**0.2436**
	SD	**0.00254**	**0.05045**	**0.03281**	**0.13053**	**0.25212**	**0.01542**	**0.05420**	**0.01955**	**0.02656**
	04-177	0.021	0.814	0.324	0.733	4.136	0.237	1.105	0.177	0.181
2.13 mg/kg	04-187	0.022	0.740	0.357	0.719	4.362	0.226	1.217	0.166	0.251
	04-200	0.023	0.882	0.325	0.709	3.916	0.241	1.271	0.182	0.236
	04-209	0.010	0.833	0.310	0.764	4.151	0.220	1.264	0.186	0.221
	04-215	0.023	0.751	0.307	0.739	4.320	0.232	1.195	0.156	0.273
	04-217	0.024	0.823	0.323	0.759	4.359	0.224	1.241	0.178	0.274
	Mean	**0.0206**	**0.8073**	**0.3244**	**0.7373**	**4.2073**	**0.2299**	**1.2155**	**0.1742**	**0.2393**
	SD	**0.00508**	**0.05321**	**0.01785**	**0.02156**	**0.17459**	**0.00820**	**0.06110**	**0.01101**	**0.03525**
	04-181	0.019	0.789	0.338	0.728	4.268	0.228	1.197	0.162	0.259
4.25 mg/kg	04-183	0.021	0.871	0.340	0.737	4.273	0.230	1.311	0.177	0.258
	04-205	0.027	0.943	0.363	0.798	4.026	0.233	1.389	0.166	0.280
	04-208	0.018	0.793	0.319	0.784	4.366	0.237	1.267	0.142	0.270
	04-210	0.019	0.828	0.317	0.724	4.452	0.235	1.262	0.196	0.255
	04-220	0.024	0.802	0.326	0.727	4.599	0.224	1.229	0.156	0.255
	Mean	**0.0211**	**0.8377**	**0.3336**	**0.7497**	**4.3307**	**0.2312**	**1.2760**	**0.1665**	**0.2628**
	SD	**0.00359**	**0.05981**	**0.01707**	**0.03272**	**0.19411**	**0.00481**	**0.06716**	**0.01861**	**0.01005**
	04-173	0.025	0.826	0.324	0.808	4.455	0.249	1.286	0.188	0.239
8.50 mg/kg	04-174	0.021	0.994	0.364	0.775	3.960	0.243	1.277	0.173	0.193
	04-189	0.026	0.874	0.333	0.792	4.184	0.232	1.372	0.198	0.251
	04-190	0.025	0.841	0.319	0.750	4.441	0.214	1.300	0.162	0.253
	04-199	0.025	0.849	0.316	0.751	4.462	0.231	1.209	0.196	0.237
	04-212	0.024	0.994	0.328	0.822	4.222	0.228	1.367	0.129	0.282
	Mean	**0.0243**	**0.8965**	**0.3306**	**0.7829**	**4.2873**	**0.2327**	**1.3019**	**0.1745**	**0.2425**
	SD	**0.00180**	**0.07735**	**0.01764**	**0.02967**	**0.20242**	**0.01227**	**0.06099**	**0.02610**	**0.02898**
	04-179	0.021	0.785	0.318	0.827	4.206	0.220	1.341	0.150	0.262
17.00 mg/kg	04-193	0.024	0.954	0.328	0.774	4.497	0.241	1.292	0.210	0.231
	04-195	0.024	1.011	0.322	0.802	3.927	0.243	1.096	0.203	0.158
	04-201	0.023	0.890	0.338	0.733	4.595	0.252	1.195	0.201	0.210
	04-202	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-204	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	Mean	**0.0232**	**0.9102**	**0.3265**	**0.7843**	**4.3062**	**0.2390**	**1.2312**	**0.1912**	**0.2150**
	SD	**0.00130**	**0.09692**	**0.00883**	**0.04021**	**0.30241**	**0.01383**	**0.10859**	**0.02880**	**0.04353**
	04-178	0.023	0.869	0.319	0.761	5.160	0.235	1.042	0.177	0.176
25.50 mg/kg	04-180	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-184	0.020	0.905	0.402	0.745	4.503	0.258	1.231	0.175	0.235
	04-207	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-213	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-219	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	Mean	**0.0218**	**0.8865**	**0.3604**	**0.7528**	**4.8311**	**0.2464**	**1.1368**	**0.1764**	**0.2055**
	SD	**0.00231**	**0.02546**	**0.05817**	**0.01104**	**0.46464**	**0.01650**	**0.13369**	**0.00156**	**0.04226**
	04-175	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
34.00 mg/kg	04-182	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-191	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-198	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-203	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-206	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	Mean									
	SD									
	04-172	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
42.50 mg/kg	04-176	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-188	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-211	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-214	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-216	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	Mean									
	SD									

= No data
(f) = Animal died on study

Table I-10
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

14-Day Individual Organ Weights (grams)
Female Rats

% Body Weight

Group	Animal ID	Adrenals	Brain	Heart	Kidneys	Liver	Ovaries	Spleen	Thymus	Uterus
	04-249	0.036	1.182		0.823	4.005	0.077	0.263	0.260	0.176
Methylcellulose	04-253	0.039	1.146	0.369	0.775	3.579	0.064	0.253	0.217	0.134
Control	04-260	0.044	1.223	0.376	0.780	3.668	0.063	0.259	0.258	0.151
	04-262	0.045	1.067	0.430	0.835	4.035	0.090	0.291	0.236	0.335
	04-272	0.047	1.064	0.389	0.794	4.196	0.064	0.239	0.222	0.247
	04-273	0.038	1.073	0.380	0.797	4.004	0.087	0.254	0.194	0.212
	Mean	**0.0415**	**1.1257**	**0.3889**	**0.8007**	**3.9146**	**0.0742**	**0.2599**	**0.2313**	**0.2091**
	SD	**0.00452**	**0.06781**	**0.02414**	**0.02377**	**0.23811**	**0.01222**	**0.01749**	**0.02552**	**0.07399**
	04-237	0.037	1.199	0.411	0.839	3.842	0.056	0.244	0.249	0.269
2.13 mg/kg	04-241	0.032	1.079	0.403	0.798	4.060	0.067	0.293	0.264	0.354
	04-247	0.044	1.101	0.418	0.753	4.043	0.076	0.292	0.242	0.218
	04-274	0.036	1.078	0.378	0.788	3.978	0.071	0.249	0.240	0.200
	04-279	0.034	1.116	0.345	0.851	3.874	0.069	0.263	0.203	0.253
	04-281	0.032	1.146	0.357	0.789	4.058	0.079	0.274	0.280	0.184
	Mean	**0.0356**	**1.1197**	**0.3852**	**0.8031**	**3.9758**	**0.0695**	**0.2691**	**0.2463**	**0.2463**
	SD	**0.00456**	**0.04636**	**0.03020**	**0.03593**	**0.09649**	**0.00808**	**0.02083**	**0.02598**	**0.06162**
	04-239	0.048	1.123	0.399	0.771	3.674	0.079	0.265	0.240	0.211
4.25 mg/kg	04-243	0.033	1.217	0.401	0.828	3.777	0.071	0.291	0.249	0.164
	04-244	0.028	1.098	0.413	0.826	4.038	0.063	0.266	0.170	0.173
	04-268		1.120	0.397	0.812	3.910	0.087	0.250	0.217	0.226
	04-269	0.038	1.111	0.433	0.791	3.897	0.063	0.284	0.211	0.172
	04-271	0.040	1.092	0.401	0.783	3.921	0.076	0.293	0.258	0.198
	Mean	**0.0375**	**1.1268**	**0.4073**	**0.8018**	**3.8695**	**0.0730**	**0.2747**	**0.2243**	**0.1908**
	SD	**0.00758**	**0.04565**	**0.01372**	**0.02382**	**0.12670**	**0.00943**	**0.01696**	**0.03209**	**0.02474**
	04-233	0.048	1.303	0.341	0.812	3.427	0.042	0.238	0.187	0.127
8.50 mg/kg	04-234	0.030	1.135	0.386	0.816	3.911	0.059	0.255	0.232	0.131
	04-242	0.035	1.209	0.392	0.808	3.690	0.072	0.262	0.220	0.198
	04-246	0.041	1.152	0.345	0.783	3.553	0.075	0.240	0.211	0.122
	04-259	0.040	1.194	0.371	0.876	3.878	0.069	0.269	0.233	0.280
	04-263	0.041	1.237	0.403	0.818	3.624	0.063	0.253	0.228	0.105
	Mean	**0.0391**	**1.2050**	**0.3730**	**0.8188**	**3.6806**	**0.0631**	**0.2527**	**0.2183**	**0.1604**
	SD	**0.00599**	**0.06076**	**0.02556**	**0.03083**	**0.18754**	**0.01204**	**0.01213**	**0.01733**	**0.06664**
	04-238	0.034	1.093	0.426	0.794	3.939	0.068	0.307	0.228	0.125
17.00 mg/kg	04-248	0.035	1.150	0.353	0.818	3.817	0.061	0.274	0.213	0.136
	04-252	0.036	1.154	0.353	0.857	4.181	0.070	0.267	0.130	0.122
	04-256	0.036	1.138	0.366	0.801	3.718	0.054	0.268	0.196	0.119
	04-264	0.039	1.090	0.392	0.821	3.908	0.089	0.295	0.189	0.168
	04-275	0.028	1.053	0.331	0.767	3.735	0.062	0.278	0.209	0.097
	Mean	**0.0347**	**1.1132**	**0.3702**	**0.8096**	**3.8832**	**0.0673**	**0.2814**	**0.1942**	**0.1280**
	SD	**0.00356**	**0.04039**	**0.03382**	**0.03038**	**0.17083**	**0.01216**	**0.01594**	**0.03449**	**0.02324**
	04-240	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
25.50 mg/kg	04-261	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-266	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-270	0.045	1.095	0.406	0.813	3.802	0.042	0.238	0.161	0.227
	04-276	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-280	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	Mean	**0.0450**	**1.0947**	**0.4060**	**0.8126**	**3.8020**	**0.0424**	**0.2384**	**0.1609**	**0.2272**
	SD	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
	04-232	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
34.00 mg/kg	04-250	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-251	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-257	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-258	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-277	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	Mean									
	SD									
	04-236	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
42.50 mg/kg	04-245	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-254	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-255	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-265	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-267	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	Mean									
	SD									

- = No data
(f) = Animal died on study

Table I-11
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

14-Day Individual Organ Weights (grams)
Male Rats

% Brain Weight

Group	Animal ID	Adrenals	Heart	Kidneys	Liver	Spleen	Testes	Thymus	Epididymides
	04-185	2.162	45.946	100.000	579.459	31.892	167.568	20.703	34.054
Methylcellulose	04-186	2.542	36.723	89.831	481.356	24.859	137.853	22.599	25.424
Control	04-192	2.458	35.754	121.788	486.592	25.698	141.899	18.994	26.816
	04-194	2.554	45.109	84.239	491.304	28.261	133.152	18.370	26.196
	04-196	2.432	36.378	94.054	497.838	25.405	153.514	17.892	29.568
	04-221	2.941	39.198	101.604	611.230	26.578	154.545	18.930	36.203
	Mean	**2.5151**	**39.8514**	**98.5859**	**524.6300**	**27.1155**	**148.0885**	**19.5813**	**29.7100**
	SD	**0.25238**	**4.55729**	**13.05725**	**55.95312**	**2.62453**	**12.78060**	**1.75805**	**4.47555**
	04-177	2.632	39.766	90.058	507.953	29.064	135.731	21.696	22.222
2.13 mg/kg	04-187	2.931	48.276	97.126	589.080	30.460	164.368	22.414	33.908
	04-200	2.626	36.872	80.447	444.134	27.374	144.134	20.670	26.816
	04-209	1.245	37.238	91.681	498.019	26.372	151.669	22.298	26.486
	04-215	3.094	40.884	98.343	575.138	30.884	159.116	20.829	36.354
	04-217	2.873	39.227	92.265	529.834	27.238	150.829	21.657	33.260
	Mean	**2.5667**	**40.3770**	**91.6534**	**524.0266**	**28.5654**	**150.9745**	**21.5940**	**29.8408**
	SD	**0.67215**	**4.15899**	**6.37499**	**53.28353**	**1.85497**	**10.25013**	**0.72392**	**5.46076**
	04-181	2.389	42.778	92.222	540.556	28.889	151.667	20.556	32.778
4.25 mg/kg	04-183	2.418	39.011	84.615	490.659	26.374	150.549	20.330	29.670
	04-205	2.857	38.462	84.615	426.923	24.725	147.253	17.582	29.670
	04-208	2.228	40.217	98.913	550.543	29.891	159.783	17.935	34.076
	04-210	2.240	38.251	87.432	537.705	28.415	152.459	23.716	30.820
	04-220	2.967	40.659	90.659	573.626	27.967	153.297	19.396	31.758
	Mean	**2.5166**	**39.8964**	**89.7428**	**520.0021**	**27.7102**	**152.5012**	**19.9190**	**31.4621**
	SD	**0.31761**	**1.70507**	**5.45899**	**53.04503**	**1.86579**	**4.14018**	**2.22084**	**1.75984**
	04-173	3.068	39.205	97.727	539.205	30.114	155.682	22.727	28.977
8.50 mg/kg	04-174	2.093	36.628	77.907	398.256	24.419	128.488	17.442	19.419
	04-189	2.928	38.122	90.608	478.453	26.519	156.906	22.652	28.729
	04-190	2.919	37.892	89.189	528.108	25.405	154.595	19.243	30.054
	04-199	2.984	37.173	88.482	525.654	27.225	142.408	23.141	27.906
	04-212	2.458	32.961	82.682	424.581	22.905	137.430	13.017	28.324
	Mean	**2.7418**	**36.9966**	**87.7657**	**482.3762**	**26.0979**	**145.9182**	**19.7037**	**27.2348**
	SD	**0.38284**	**2.16314**	**6.82484**	**59.37304**	**2.49273**	**11.65767**	**3.99236**	**3.89737**
	04-179	2.738	40.476	105.357	535.714	27.976	170.833	19.048	33.333
17.00 mg/kg	04-193	2.527	34.409	81.183	471.505	25.269	135.484	22.043	24.194
	04-195	2.402	31.844	79.330	388.268	24.022	108.380	20.112	15.642
	04-201	2.567	37.968	82.353	516.043	28.342	134.225	22.620	23.529
	04-202	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-204	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	Mean	**2.5585**	**36.1741**	**87.0556**	**477.8826**	**26.4024**	**137.2304**	**20.9557**	**24.1747**
	SD	**0.13874**	**3.81209**	**12.26434**	**65.50349**	**2.09678**	**25.64887**	**1.66396**	**7.23640**
	04-178	2.703	36.757	87.568	594.054	27.027	120.000	20.432	20.216
25.50 mg/kg	04-180	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-184	2.233	44.389	82.356	497.767	28.532	136.125	19.375	26.019
	04-207	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-213	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-219	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	Mean	**2.4680**	**40.5727**	**84.9619**	**545.9103**	**27.7793**	**128.0625**	**19.9035**	**23.1176**
	SD	**0.33185**	**5.39653**	**3.68498**	**68.08550**	**1.06386**	**11.40215**	**0.74796**	**4.10318**
	04-175	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
34.00 mg/kg	04-182	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-191	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-198	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-203	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-206	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	Mean								
	SD								
	04-172	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
42.50 mg/kg	04-176	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-188	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-211	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-214	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-216	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	Mean								
	SD								

(f) = Animal died on study

Table I-12
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

14-Day Individual Organ Weights (grams)
Female Rats

% Brain Weight

Group	Animal ID	Adrenals	Heart	Kidneys	Liver	Ovaries	Spleen	Thymus	Uterus
	04-249	3.014		69.681	339.014	6.551	22.261	22.029	14.899
Methylcellulose	04-253	3.416	32.195	67.615	312.397	5.629	22.075	18.975	11.701
Control	04-260	3.621	30.783	63.785	299.942	5.140	21.203	21.086	12.325
	04-262	4.247	40.287	78.201	378.014	8.432	27.295	22.111	31.355
	04-272	4.391	36.611	74.644	394.434	5.999	22.449	20.903	23.253
	04-273	3.540	35.398	74.336	373.274	8.083	23.658	18.053	19.764
	Mean	**3.7049**	**29.2123**	**71.3772**	**349.5126**	**6.6390**	**23.1568**	**20.5263**	**18.8829**
	SD	**0.52141**	**14.69954**	**5.30405**	**38.31430**	**1.34039**	**2.17579**	**1.65818**	**7.56167**
	04-237	3.080	34.323	69.989	320.549	4.647	20.381	20.773	22.452
2.13 mg/kg	04-241	2.923	37.376	73.943	376.182	6.219	27.114	24.440	32.774
	04-247	3.979	37.931	68.435	367.308	6.897	26.525	21.950	19.761
	04-274	3.331	35.039	73.171	369.185	6.544	23.081	22.249	18.560
	04-279	3.028	30.890	76.257	347.244	6.178	23.561	18.231	22.714
	04-281	2.764	31.143	68.857	353.931	6.880	23.894	24.447	16.032
	Mean	**3.1842**	**34.4501**	**71.7753**	**355.7331**	**6.2274**	**24.0929**	**22.0150**	**22.0489**
	SD	**0.43197**	**2.98832**	**3.14935**	**20.23026**	**0.83337**	**2.45645**	**2.35438**	**5.81775**
	04-239	4.271	35.570	68.639	327.273	7.016	23.612	21.415	18.792
4.25 mg/kg	04-243	2.740	32.936	68.017	310.423	5.837	23.883	20.429	13.520
	04-244	2.526	37.603	75.264	367.744	5.699	24.266	15.511	15.746
	04-268		35.414	72.520	349.008	7.760	22.287	19.370	20.187
	04-269	3.434	38.958	71.226	350.740	5.684	25.518	19.005	15.512
	04-271	3.688	36.755	71.666	359.066	6.945	26.798	23.663	18.132
	Mean	**2.7765**	**36.2061**	**71.2220**	**344.0422**	**6.4902**	**24.3939**	**19.8990**	**16.9814**
	SD	**1.50125**	**2.07593**	**2.65208**	**21.30010**	**0.87159**	**1.57289**	**2.72328**	**2.47147**
	04-233	3.663	26.163	62.326	263.023	3.198	18.256	14.360	9.767
8.50 mg/kg	04-234	2.655	34.037	71.937	344.599	5.190	22.511	20.398	11.527
	04-242	2.892	32.447	66.802	305.147	5.957	21.631	18.161	16.368
	04-246	3.522	29.937	67.925	308.365	6.478	20.818	18.302	10.566
	04-259	3.377	31.039	73.377	324.870	5.779	22.532	19.481	23.442
	04-263	3.316	32.577	66.143	293.077	5.061	20.419	18.441	8.493
	Mean	**3.2374**	**31.0333**	**68.0848**	**306.5136**	**5.2772**	**21.0277**	**18.1905**	**13.3605**
	SD	**0.38617**	**2.76871**	**4.03623**	**27.80169**	**1.14324**	**1.60782**	**2.06319**	**5.62926**
	04-238	3.129	38.929	72.623	360.289	6.197	28.039	20.878	11.432
17.00 mg/kg	04-248	3.040	30.699	71.125	331.854	5.289	23.830	18.541	11.854
	04-252	3.083	30.599	74.287	362.420	6.108	23.153	11.227	10.588
	04-256	3.129	32.190	70.337	326.655	4.753	23.526	17.208	10.469
	04-264	3.600	36.005	75.319	358.537	8.188	27.062	17.364	15.389
	04-275	2.687	31.403	72.776	354.567	5.851	26.388	19.821	9.254
	Mean	**3.1112**	**33.3042**	**72.7446**	**349.0536**	**6.0644**	**25.3328**	**17.5066**	**11.4976**
	SD	**0.29197**	**3.40265**	**1.86797**	**15.63812**	**1.17441**	**2.08320**	**3.38623**	**2.10692**
	04-240	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
25.50 mg/kg	04-261	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-266	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-270	4.114	37.084	74.229	347.308	3.872	21.779	14.701	20.750
	04-276	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-280	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	Mean	**4.1137**	**37.0841**	**74.2287**	**347.3079**	**3.8717**	**21.7786**	**14.7005**	**20.7502**
	SD	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
	04-232	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
34.00 mg/kg	04-250	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-251	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-257	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-258	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-277	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	Mean								
	SD								
	04-236	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
42.50 mg/kg	04-245	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-254	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-255	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-265	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-267	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	Mean								
	SD								

= No data
(f) = Animal died on study

APPENDIX J

SUMMARY OF 14-DAY CLINICAL CHEMISTRY AND INDIVIDUAL CLINICAL CHEMISTRY DATA

Table J-1
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Summary of Clinical Chemistry
Male Rats

		Methylcellulose Control	RDX in 1% Methylcellulose / 0.2% Tween 80						
			2.13 mg/kg	4.25 mg/kg	8.50 mg/kg	17.00 mg/kg	25.50 mg/kg	34.00 mg/kg	42.50 mg/kg
ALK P	Mean	256.2	232.2	249.5	286.3	192.3	239.5	(f)	(f)
(U/L)	S.D.	52.80	48.99	49.46	82.37	54.64	4.95		
	N	6	6	6	4	4	2		
ALT	Mean	74.5	86.5	402.7	227.0	71.0	139.0	(f)	(f)
(U/L)	S.D.	32.92	60.89	760.59	356.35	47.22	101.82		
	N	6	6	6	4	4	2		
AST	Mean	257.5	325.3	697.0	497.0	373.8	511.0	(f)	(f)
(U/L)	S.D.	202.52	223.74	920.02	392.71	413.36	43.84		
	N	6	6	6	4	4	2		
BUN	Mean	26.43	26.60	27.23	27.70	25.98	27.00	(f)	(f)
(mg/dL)	S.D.	1.349	1.602	2.341	0.883	1.531	1.273		
	N	6	6	6	4	4	2		
Ca	Mean	10.960	10.705	10.995	10.633	10.640	10.700	(f)	(f)
(mg/dL)	S.D.	0.3953	0.3297	0.7108	0.4012	0.2149	0.4950		
	N	6	6	6	4	4	2		
CHOL	Mean	74.90	78.40	75.72	78.88	73.70	69.70	(f)	(f)
(mg/dL)	S D.	10.939	5.942	4.897	8.100	6.563	1.131		
	N	6	6	6	4	4	2		
CK	Mean	3205.6	3286.3	4487.4	1924.3	3296.0	4285.5	(f)	(f)
(U/L)	S.D.	3383.82	2165.84	3107.02	1218.34	3280.21	471.64		
	N	5	3	5	3	4	2		
CREA	Mean	0.348	0.328	0.332	0.283	0.348	0.330	(f)	(f)
(mg/dL)	S.D.	0.0382	0.0515	0.0608	0.0665	0.0275	0.0141		
	N	6	6	6	4	4	2		
GLU	Mean	225.38	205.80	240.10	193.83	198.50	212.10	(f)	(f)
(mg/dL)	S.D.	33.309	18.961	43.218	8.410	34.335	2.263		
	N	6	6	6	4	4	2		
LDH	Mean	2833.8	3644.3	4867.8	4426.5	5446.3	6121.5	(f)	(f)
(U/L)	S.D.	2831.97	4033.69	4307.97	4603.09	4075.78	656.90		
	N	6	3	5	4	4	2		
TBIL	Mean	0.192	0.367	0.312	0.713	0.393	0.195	(f)	(f)
(mg/dL)	S.D.	0.2197	0.4383	0.1879	0.9841	0.2016	0.1061		
	N	6	6	6	4	4	2		
TP	Mean	5.737	5.837	5.798	6.065	5.763	5.785	(f)	(f)
(g/dL)	S.D.	0.1792	0.1888	0.1659	0.5043	0.3513	0.1202		
	N	6	6	6	4	4	2		
TRIG	Mean	159.55	171.58	172.33	172.43	124.98	139.50	(f)	(f)
(mg/dL)	S.D.	32.042	46.536	19.241	22.928	41.675	26.587		
	N	6	6	6	4	4	2		
Na	Mean	145.50	145.54	145 70	146.22	146.20	146.55	(f)	(f)
(mmol/L)	S.D.	1.550	1.230	2.605	2.689	1.080	0.354		
	N	6	5	6	5	4	2		
K	Mean	5.787	5.812	6.915	5.566	6.823	6.150	(f)	(f)
(mmol/L)	S.D.	0.9593	0.7524	1.5842	1.1157	1.1389	0.0707		
	N	6	5	6	5	4	2		
Cl	Mean	104.38	105.24	105.00	104.98	105.00	105.35	(f)	(f)
(mmml/L)	S.D.	1.068	0.518	0.701	0.444	0.616	0.071		
	N	6	5	6	5	4	2		

(f) = All animals died on study

Table J-2
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Summary of Clinical Chemistry
Female Rats

		Methylcellulose	RDX in 1% Methylcellulose / 0.2% Tween 80						
		Control	2.13 mg/kg	4.25 mg/kg	8.50 mg/kg	17.00 mg/kg	25.50 mg/kg	34.00 mg/kg	42.50 mg/kg
ALK P	Mean	215.8	203.3	188.5	230.7	250.0	194.0	(f)	(f)
(U/L)	S.D.	55.27	26.04	36.49	29.19	18.17	0		
	N	5	6	6	6	6	1		
ALT	Mean	750.0	151.0	215.3	91.3	278.8	61.0	(f)	(f)
(U/L)	S.D.	1340.88	79.45	309.79	35.80	408.46	0		
	N	5	6	6	6	6	1		
AST	Mean	1144.0	408.7	529.8	330.7	422.2	329.0	(f)	(f)
(U/L)	S.D.	1606.74	185.40	396.84	137.54	465.79	0		
	N	5	6	6	6	6	1		
BUN	Mean	27.10	27.43	27.72	27.68	25.98	23.10	(f)	(f)
(mg/dL)	S.D.	1.840	2.336	2.970	1.670	1.312	0		
	N	5	6	6	6	6	1		
Ca	Mean	9.994	10.390	10.283	10.383	10.833	10.080	(f)	(f)
(mg/dL)	S.D.	0.6024	0.2614	0.5621	0.6841	0.3478	0		
	N	5	6	6	6	6	1		
CHOL	Mean	73.60	80.97	82.48	88.07*	74.98	80.70	(f)	(f)
(mg/dL)	S.D.	5.828	1.895	7.609	8.959	5.427	0		
	N	5	6	6	6	6	1		
CK	Mean	2193.3	3098.2	3566.2	3051.5	2073.8	2349.0	(f)	(f)
(U/L)	S.D.	922.28	1984.52	2389.57	1799.36	1330.10	0		
	N	4	5	6	6	6	1		
CREA	Mean	0.340	0.305	0.352	0.340	0.332	0.320	(f)	(f)
(mg/dL)	S.D.	0 0394	0.0489	0.0371	0.0352	0.0366	0		
	N	5	6	6	6	6	1		
GLU	Mean	234.14	225.92	204.37	193.87	212.13	182.40	(f)	(f)
(mg/dL)	S.D.	25.154	21.882	24.057	31.909	21.570	0		
	N	5	6	6	6	6	1		
LDH	Mean	5969.8	5767.2	5478.0	4153.8	4024.7	3787.0	(f)	(f)
(U/L)	S.D.	3611.43	2126.28	3103.10	1656.50	3833.48	0		
	N	5	6	6	6	6	1		
TBIL	Mean	0.400	0.232	0.295	0.215	0.140	0.100	(f)	(f)
(mg/dL)	S.D.	0.6708	0.2409	0.2536	0.1764	0.0980	0		
	N	5	6	6	6	6	1		
TP	Mean	5.472	5.480	5.620	5.703	5.387	5.690	(f)	(f)
(g/dL)	S.D.	0.4298	0.3413	0.1779	0.2875	0.2422	0		
	N	5	6	6	6	6	1		
TRIG	Mean	82.92	78.83	82.65	90.22	72.57	60.20	(f)	(f)
(mg/dL)	S.D.	28.528	27.491	26.047	22.627	20.595	0		
	N	5	6	6	6	6	1		
Na	Mean	143.84	145.24	144.83	147.22	146.52	146.40	(f)	(f)
(mmol/L)	S.D.	3.715	0.820	2.381	2.218	1.322	0		
	N	5	5	6	6	5	1		
K	Mean	6.396	5.736	6.077	5.972	6.036	6.090	(f)	(f)
(mmol/L)	S.D.	3.4078	0.2883	0.8988	0.4893	1.3980	0		
	N	5	5	6	6	5	1		
Cl	Mean	104.66	106.26	105.28	105.70	104.80	104.00	(f)	(f)
(mmml/L)	S.D.	0.871	1.623	1.146	0.514	0.292	0		
	N	5	5	6	6	5	1		

(f) = All animals died on study
* p less than or equal to 0.05
ANOVA with Holm-Sidak Method

Table J-3
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

14-Day Individual Clinical Chemistry
Male Rats

Group	Animal ID	ALKP (U/L)	ALT (U/L)	AST (U/L)	BUN (mg/dL)	CA (mg/dL)	CHOL (mg/dL)	CK (U/L)	CREA (mg/dL)	GLU (mg/dL)	LDH (U/L)	TBIL (mg/dL)	TP (g/dL)	TRIG (mg/dL)	Na (mmol/L)	K (mmol/L)	Cl (mmol/L)	Comments
	04-185	316	50	199	26 2	10 96	63 1	1180	0 34	251 8	1601	0 11	5 53	124 2	145 9	4 99	103 7	
Methylcellulose	04-186	162	92	595	26.2	10 76	75 3	8144	0 30	212 1	8032	0 64	5 99	187 7	145 3	7 30	106 3	SS, 1 3 dilution for LDH, CK
Control	04-192	259	54	112	25 0	10 88	90 7	745	0 36	196 5	1151	0 10	5.89	149 0	145.9	6 67	103 9	
	04-194	266	134	414	28 5	11 73	84 4	5341	0 41	280 3	4225	0 10	5 59	130 4	148 0	5 37	103.8	1 3 dilution for LDH, CK
	04-196	291	54	108	27.5	10 61	71 3		0 36	200 5	848	0 10	5 65	160 3	143 4	5 09	103 6	SS no CK
	04-221	243	63	117	25 2	10 82	64.6	618	0.32	211 1	1146	0 10	5 77	205 7	144 5	5 30	105.0	
	Mean	**256.2**	**74.5**	**257.5**	**26.43**	**10.960**	**74.90**	**3205.6**	**0.348**	**225.38**	**2833.8**	**0.192**	**5.737**	**159.55**	**145.50**	**5.787**	**104.38**	
	SD	**52.80**	**32.92**	**202.52**	**1.349**	**0.3953**	**10.939**	**3383.82**	**0.0382**	**33.309**	**2831.97**	**0.2197**	**0.1792**	**32.042**	**1.950**	**0.9593**	**1.068**	
	04-177	230	65	319	26 3	10 59	84 6		0 35	204.0		0 10	5 72	190 7	146 0	5 21	104 6	SS, no dilutions or CK
2.13 mg/kg	04-187	261	44	75	25 9	11 05	79 9	797	0 37	203 3	735	0 10	5 76	184 9	145 5	5.81	105 8	
	04-200	225	188	634	26 3	11 00	70 4	4323	0 31	229 4	8249	0 34	5 63	100 9	145 4	5 92	105 6	1 3 dilution for LDH, CK
	04-209	154	132	534	29 8	10 14	71 6	4739	0 25	214 9		1 23	6 00	141 0	143 7	7 00	105 4	SS, slightly hemolyzed, 1 3 dilution LDH, CK
	04-215	302	30	109	25 9	10 77	82 4		0 30	172 3	1949	0 33	6 13	237 5				SS, no CK or electrolytes
	04-217	221	60	281	25 4	10 68	81 5		0 39	210 9		0 10	5 78	174 5	147 1	5 12	104 8	SS, no LDH or CK
	Mean	**232.2**	**84.5**	**335.3**	**26.60**	**10.705**	**78.40**	**3286.3**	**0.328**	**205.80**	**3444.3**	**0.367**	**5.837**	**171.58**	**145.54**	**5.812**	**105.24**	
	SD	**48.99**	**60.09**	**223.74**	**1.602**	**0.3297**	**5.942**	**2165.84**	**0.0515**	**18.961**	**4033.69**	**0.4363**	**0.1888**	**46.536**	**1.230**	**0.7534**	**0.518**	
	04-181	252	296	1025	27 7	12.10	73.5	4771	0 35	278.8		0 10	5 81	174 1	148 2	7 25	106 3	SS; 1 3 dilution LDH, CK
4.25 mg/kg	04-183	272	46	136	26 4	10 88	73 7		0 42	222 7	1195	0.10	5 57	145 4	148 1	5 64	105.0	SS, no CK
	04-205	256	1941	2436	26 1	11.30	76 1	8144	0.25	304.0	11200	0 34	5 81	157 9	143 5	9 77	104 7	SS, 1 3 dilution LDH, CK
	04-208	322	10	71	29 6	10 32	81.2	685	0 31	206 2	1006	0 43	5 91	181 5	147 6	5 37	104 2	
	04-210	175	46	315	29 9	10.16	81 2	6731	0 29	192 2	7052	0 58	6 03	174 0	144 6	7 05	104 8	slightly hemolyzed, 1 3 dilution LDH, CK
	04-220	220	77	199	23 7	11 21	68 6	2106	0 37	236 7	3886	0 32	5 66	201.1	142 2	6 41	105 0	1 3 dilution for LDH, CK
	Mean	**249.5**	**402.7**	**697.0**	**27.23**	**10.995**	**75.72**	**4487.4**	**0.332**	**240.10**	**4867.8**	**0.312**	**5.798**	**172.33**	**145.70**	**6.915**	**105.00**	
	SD	**49.46**	**760.59**	**920.82**	**2.341**	**0.7108**	**4.897**	**3107.02**	**0.0608**	**43.218**	**4307.97**	**0.1879**	**0.1659**	**19.241**	**2.605**	**1.5842**	**0.701**	
	04-173	234	83	359	26 9	10 38	69 6	2036	0 34	190 5	2800	0 21	5 76	189.7	144 9	5 76	105.0	SS, no dilutions
8.50 mg/kg	04-174	409	17	492	27 2	10 21	89 2		0 19	183.8	2800	2.18	6 74	173 5	150 9	6 16	105 3	SS, no dilutions or CK
	04-189	245	760	1034	27 8	10 89	77 0	3083	0.28	202 9	11200	0 36	6 15	139 7	145 7	7 01	105 5	SS, 1 3 dilution LDH, CK
	04-190	257	48	103	28 9	11 05	79 7	654	0 32	198 1	906	0 10	5 61	186 8	144 1	4 53	104 7	
	04-199														145 5	4.37	104 4	SS, fibrin error, electrolytes only
	04-212																	
	Mean	**286.3**	**227.0**	**497.0**	**27.70**	**10.633**	**78.88**	**1924.3**	**0.283**	**193.83**	**4426.5**	**0.713**	**6.065**	**172.43**	**146.22**	**5.566**	**104.98**	
	SD	**82.37**	**356.35**	**392.73**	**0.883**	**0.4012**	**8.100**	**1218.34**	**0.0665**	**8.410**	**4603.09**	**0.9841**	**0.5043**	**22.928**	**2.689**	**1.1157**	**0.444**	
	04-179	146	39	154	28 1	10.34	76 9	1222	0 32	170.6	3804	0.51	5 83	76 7	147 6	7 11	105 8	1 3 dilution for LDH, CK
17.00 mg/kg	04-193	236	140	990	25 4	10.85	69 5	8144	0 38	203 5	11200	0 42	5 94	178 4	146.5	7 47	105 0	SS, 1 3 dilution LDH, CK
	04-195	144	63	230	25 9	10 67	81.3	2469	0 33	174 8	5061	0 54	6 03	124 9	145 3	7.57	104 9	1 3 dilution for LDH, CK
	04-201	243	42	121	24 5	10 70	67 1	1349	0 36	245.1	1720	0 10	5 25	119 9	145 4	5 14	104 3	
	04-202	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	04-204	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	Mean	**192.3**	**71.0**	**373.8**	**25.98**	**10.640**	**73.70**	**3296.0**	**0.348**	**198.50**	**5446.3**	**0.393**	**5.763**	**124.98**	**146.20**	**6.823**	**105.00**	
	SD	**54.64**	**47.22**	**413.36**	**1.531**	**0.2149**	**6.563**	**3280.21**	**0.0275**	**34.335**	**4075.78**	**0.2016**	**0.3513**	**41.675**	**1.080**	**1.1389**	**0.616**	
	04-178	236	67	480	26 1	10 35	68.9	4619	0.32	210.5	5657	0.27	5 70	158 3	146 3	6 20	105.3	1 3 dilution for LDH, CK
25.50 mg/kg	04-180	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	04-184	243	211	542	27 9	11 05	70.5	3952	0.34	213 7	6586	0.52	5 87	120.7	146 8	6.10	105 4	1.3 dilution for LDH, CK
	04-207	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	04-213	(f)	(f)		(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	04-219	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	Mean	**239.5**	**139.0**	**511.0**	**27.00**	**10.700**	**69.70**	**4285.5**	**0.330**	**212.10**	**6121.5**	**0.195**	**5.785**	**139.50**	**146.55**	**6.150**	**105.35**	
	SD	**4.95**	**101.82**	**43.84**	**1.273**	**0.4950**	**1.131**	**471.64**	**0.0141**	**2.263**	**656.98**	**0.1061**	**0.1202**	**26.587**	**0.354**	**0.0707**	**0.071**	
	04-175	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
34.00 mg/kg	04-182	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	04-191	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	04-198	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	04-203	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	04-206	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	Mean																	
	SD																	
	04-172	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
42.50 mg/kg	04-176	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	04-188	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	04-211	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	04-214	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	04-216	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	Mean																	
	SD																	

= No data
(f) = Animal died on study

Table J-4
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

14-Day Summary of Clinical Chemistry
Female Rats

Group	Animal ID	ALKP (U/L)	ALT (U/L)	AST (U/L)	BUN (mg/dL)	CA (mg/dL)	CHOL (mg/dL)	CK (U/L)	CREA (mg/dL)	GLU (mg/dL)	LDH (U/L)	TBIL (mg/dL)	TP (g/dL)	TRIG (mg/dL)	Na (mmol/L)	K (mmol/L)	Cl (mmol/L)	Comments
	04-249																	no sample
Methylcellulose Control	04-253	237	83	232	26 2	10 47	79 6	1348	0 31	215 7	2061	0 10	4 97	75 2	146 3	4 60	106 2	
	04-260	224	149	555	26 4	9 74	76 4	3465	0 34	225 9	6141	0 10	5 13	62 4	143 1	5 20	104 5	slightly hemolyzed, 1 3 dilution for LDH, CK
	04-262	119	3145	4003	25 7	9 05	64 8		0 30	277 5	11200	1 60	6 05	80 3	137 7	12.48	104 2	hemolyzed, 1:3 dilution for ALT, AST, LDH, CK
	04-272	255	101	304	30 3	10 42	76 3	1726	0 40	233 0	3175	0 10	5 62	132 2	146 8	4 83	104 2	slightly hemolyzed, 1 3 dilution for LDH, CK
	04-273	244	272	626	26 9	10 29	70 9	2234	0 35	218 6	7272	0 10	5 59	64 5	145 3	4 87	104 2	slightly hemolyzed, 1 3 dilution for LDH, CK
	Mean	215.8	750.0	1144 0	27.10	9.994	73.60	2193.3	0.340	234.14	5969.8	0.400	5.472	82.92	143.84	6.396	104.66	
	SD	55.27	1348.88	1606.74	1.640	0.6024	5.828	922.28	0.0394	25.154	3611.43	0.6708	0.4298	28.528	3.715	3.4078	0.871	
2.13 mg/kg	04-237	217	121	498	26 5	10 07	79 1	2468	0 30	240 3	5680	0.16	5 18	59 0	145 0	5 74	105 4	slightly hemolyzed 1 3 dilution for LDH, CK
	04-241	198	177	676	25 0	10 44	83 6	5187	0 29	263 9	7735	0 16	5 10	86 3	143.9	5 77	105 5	slightly hemolyzed, 1 3 dilution for LDH, CK
	04-247	216	300	527	25 2	10 42	82 5		0 36	212 7	8571	0 10	5 62	83 3				SS: slightly hemolyzed, 1 3 dilution for LDH
	04-274	208	95	206	28 7	10 73	80 8	984	0 32	206 6	2883	0 15	5 66	81 1	145 8	5 34	106 1	1 3 dilution for LDH, CK
	04-279	154	125	284	28 1	10 10	78 7	1650	0 22	216 1	5547	0 72	6 00	41 1	145 7	5 68	109.1	hemolyzed, 1 3 dilution for LDH, CK
	04-281	227	88	261	31 1	10.58	81 1	5202	0 34	215 9	4187	0.10	5.32	122 2	145 8	6 15	105 2	slightly hemolyzed, 1:3 dilution for LDH, CK
	Mean	203.3	151.0	408.7	27.43	10.390	80.97	3098.2	0.305	225.92	5767.2	0.232	5.480	78.83	145.24	5.736	106.26	
	SD	26.04	79.45	185.40	2.336	0.2614	1.895	1984.52	0.0489	21.882	2126.28	0.2409	0.3413	27.491	0.820	0.2883	1.623	
4.25 mg/kg	04-239	237	87	514	27 4	10 33	79 8	2991	0 39	189.8	5282	0.19	5 76	44.9	145 6	6 10	104 9	1 3 dilution for LDH, CK
	04-243	189	69	241	26 1	10.27	79 4	1693	0 38	224 3	3117	0.18	5 35	87 8	145.2	5 21	104.3	slightly hemolyzed, 1 3 dilution for LDH, CK
	04-244	150	145	516	23.1	9.68	85 6	4073	0 34	181 9	6497	0 26	5 50	92 3	144 6	6 40	105 9	hemolyzed, 1 3 dilution for LDH, CK
	04-268	204	70	337	29 9	11 30	92 6	2353	0 38	243 2	3407	0 24	5 84	112 1	148 8	5 78	107.2	slightly hemolyzed, 1 3 dilution for LDH, CK
	04-269	209	76	268	28.2	10.26	86.9	2143	0 30	189 3	3365	0 10	5 60	101 3	142 4	5 31	104 1	1 3 dilution for LDH, CK
	04-271	142	845	1303	31.6	9 86	70 6	8144	0 32	197 7	11200	0 80	5.67	57.5	142 4	7 66	105 3	1:3 dilution for AST, LDH, CK
	Mean	188.5	215.3	529.8	27.72	10.283	82.48	3566.2	0.352	204.37	5478.0	0.295	5.620	82.65	144.83	6.077	105.28	
	SD	36.49	309.79	396.84	2.970	0.5621	7.609	2389.57	0.0371	24.057	3103.10	0.2536	0.1779	26.047	2.381	0.8988	1.146	
8.50 mg/kg	04-233	248	73	343	26 8	9 98	91 8	3054	0 31	149 3	5484	0 10	5 67	79.1	148 0	5 65	105 6	slightly hemolyzed, 1 3 dilution for LDH, CK
	04-234	180	144	539	30 3	10 58	81 0	6433	0 30	200 5	6718	0 53	5 73	80.3	145 8	6 51	106 6	hemolyzed, 1:3 dilution for LDH, CK
	04-242	220	66	116	25 9	9 84	82 3	1031	0 36	180 0	2102	0 10	5 60	89 3	146 2	5 84	105 9	
	04-246	261	130	371	29 0	11 68	104 5	2782	0 39	227 7	3612	0 32	6 22	131.4	151.4	6 44	105 4	1 3 dilution for LDH, CK
	04-259	249	71	274	27 6	10 03	86 3	2489	0 36	230 8	3389	0 14	5 34	65 5	146 3	5 24	105 1	1 3 dilution for LDH, CK
	04-263	226	64	341	26 5	10.19	82.5	2520	0 32	174 9	3618	0 10	5 66	95 7	145.6	6 15	105.6	1 3 dilution for LDH, CK
	Mean	230.7	91.3	330.7	27.68	10.383	88.07	3051.5	0.340	193.87	4153.8	0.215	5.703	90.22	147.22	5.972	105.70	
	SD	29.19	35.80	137.54	1.670	0.6841	8.959	1799.36	0.0352	31.909	1656.50	0.1764	0.2875	22.627	2.218	0.4893	0.514	
17.00 mg/kg	04-238	265	44	111	24 7	10 47	73 4	789	0 36	222 0	933	0 10	5 23	75 7	146 8	4 73	104 6	
	04-248	270	303	383	27 9	10 53	68 8	1127	0 37	214 6	5115	0 10	5 43	48.3	145 9	5 71	105 0	1 3 dilution for LDH, CK
	04-252	231	66	146	24 5	10 72	78 0	2644	0 34	173 5	1692	0.10	5 49	106 0	148 7	6 08	104 5	1:3 dilution for CK
	04-256	262	82	217	26 9	10 98	72 4	1295	0 34	213 9	1664	0.10	5 10	61 6	145 4	5 29	104.7	
	04-264	244	1090	1349	25 6	11 42	84 3	4387	0 31	239 0	11200	0 34	5 79	83 8	145.8	8.37	105 2	hemolyzed; 1:3 dilution for ALT, AST, LDH, CK
	04-275	228	88	327	26 3	10 88	73	2201	0 27	209 8	3544	0.10	5.28	60				SS, no electrolytes, 1 3 dilution for LDH, CK
	Mean	250.0	278.8	422.2	25.98	10.833	74.98	2073.8	0.332	212.13	4024.7	0.140	5.387	72.57	146.52	6.036	104.80	
	SD	18.17	408.46	465.79	1.312	0.3478	5.427	1330.10	0.0366	21.570	3833.48	0.0980	0.2422	20.595	1.322	1.3980	0.292	
25.50 mg/kg	04-240	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	04-261	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	04-266	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	04-270	194	61	329	23 1	10 08	80 7	2349	0 32	182 4	3787	0.10	5 69	60 2	146 4	6 09	104 0	slightly hemolyzed, 1 3 dilution for LDH, CK
	04-276	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	04-280	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	Mean	194.0	61.0	329.0	23.10	10.080	80.70	2349.0	0.320	182.40	3787.0	0.100	5.690	60.20	146.40	6.090	104.00	
	SD	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
34.00 mg/kg	04-232	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	04-250	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	04-251	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	04-257	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	04-258	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	04-277	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	Mean																	
	SD																	
42.50 mg/kg	04-236	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	04-245	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	04-254	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	04-255	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	04-265	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	04-267	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	Mean																	
	SD																	

= No data
(f) = Animal died on study

APPENDIX K

SUMMARY OF 14-DAY HEMATOLOGY AND INDIVIDUAL HEMATOLOGY DATA

Table K-1
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Summary of Hematology
Male Rats

		Methylcellulose	RDX in 1% Methylcellulose / 0.2% Tween 80						
		Control	2.13 mg/kg	4.25 mg/kg	8.50 mg/kg	17.00 mg/kg	25.50 mg/kg	34.00 mg/kg	42.50 mg/kg
WBC	Mean	6.238	5.360	5.282	4.944	5.643	4.450	(f)	(f)
(K/uL)	S.D.	3.2184	2.1250	1.7933	0.5350	3.0659	0		
	N	5	5	6	5	4	2		
NEU	Mean	12.9040	14.3400	12.8200	13.0620	12.8500	14.8000	(f)	(f)
(%N)	S.D.	2.64085	2.23786	6.17252	2.67903	2.37276	0.98995		
	N	5	5	6	5	4	2		
LYM	Mean	84.4000	81.6000	84.6833	83.5400	84.6500	82.1000	(f)	(f)
(%L)	S.D.	3.30151	3.80592	4.88156	3.25161	2.35301	0.42426		
	N	5	5	6	5	4	2		
MONO	Mean	0.8856	2.3586	0.7892	1.6128	1.1615	1.6350	(f)	(f)
(%M)	S.D.	1.11305	2.75245	0.97192	1.10072	0.76900	0.58690		
	N	5	5	6	5	4	2		
EOS	Mean	0.7454	0.6956	0.8597	0.8186	0.5745	0.3255	(f)	(f)
(%E)	S.D.	0.36141	0.41253	0.48735	0.30929	0.14240	0.11809		
	N	5	5	6	5	4	2		
BASO	Mean	1.0374	0.9932	0.8387	0.9602	0.7970	1.1895	(f)	(f)
(%B)	S.D.	0.25067	0.37305	0.47935	0.62630	0.17819	0.69367		
	N	5	5	6	5	4	2		
RBC	Mean	8.282	8.402	7.772	8.664	8.038	7.975	(f)	(f)
(M/uL)	S.D.	0.8099	0.5322	0.8544	0.4735	0.6206	0.5445		
	N	5	5	6	5	4	2		
HGB	Mean	14.02	14.14	13.10	14.73	13.78	13.40	(f)	(f)
(g/dL)	S.D.	1.197	0.991	1.387	0.596	1.486	0.566		
	N	5	5	6	5	4	2		
HCT	Mean	41.34	42.46	39.12	43.44	40.80	40.00	(f)	(f)
(%)	S.D.	3.606	2.200	4.304	2.444	2.714	2.828		
	N	5	5	6	5	4	2		
MCV	Mean	49.94	50.54	50.33	50.14	50.85	50.10	(f)	(f)
(fL)	S.D.	0.639	0.635	0.398	0.152	0.624	0.141		
	N	5	5	6	5	4	2		
MCH	Mean	18.00	18.18	17.92	17.98	18.20	18.30	(f)	(f)
(pg)	S.D.	0.374	0.319	0.479	0.130	0.424	0.141		
	N	5	5	6	5	4	2		
MCHC	Mean	36.04	36.00	35.58	35.82	35.85	36.50	(f)	(f)
(g/dL)	S.D.	0.422	0.447	1.019	0.277	0.500	0.283		
	N	5	5	6	5	4	2		
RDW	Mean	13.96	14.20	13.65	14.54	13.75	13.45	(f)	(f)
(%)	S.D.	0.669	0.612	0.853	0.555	0.794	0.495		
	N	5	5	6	5	4	2		
PLT	Mean	580.88	540.38	519.17	768.60	501.93	329.90	(f)	(f)
(K/uL)	S.D.	361.858	382.436	407.453	241.015	483.030	374.908		
	N	5	5	6	5	4	2		
MPV	Mean	9.675	10.006	10.085	9.946	9.828	10.040	(f)	(f)
(fL)	S.D.	0.4397	0.8525	0.5517	0.6150	1.1316	0.9334		
	N	4	5	4	5	4	2		

(f) = All animals died on study

Table K-2
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Summary of Hematology
Female Rats

		Methylcellulose Control	RDX in 1% Methylcellulose / 0.2% Tween 80						
			2.13 mg/kg	4.25 mg/kg	8.50 mg/kg	17.00 mg/kg	25.50 mg/kg	34.00 mg/kg	42.50 mg/kg
WBC	Mean	4.645	5.374	4.798	4.778	5.628		(f)	(f)
(K/uL)	S.D.	2.6652	3.0303	1.2041	0.6368	1.3254			
	N	4	6	4	4	5	1		
NEU	Mean	26.9000	22.7567	12.4000	15.2250	12.7160		(f)	(f)
(%N)	S.D.	30.07158	25.54032	3.16965	3.16056	4.71465			
	N	4	6	4	4	5	1		
LYM	Mean	66.3500	72.8833	84.8500	82.6750	84.8400		(f)	(f)
(%L)	S.D.	35.97152	29.94284	3.20884	2.95790	5.42476			
	N	4	6	4	4	5	1		
MONO	Mean	4.3238	2.2920	0.9908	0.4465	1.0810		(f)	(f)
(%M)	S.D.	4.62166	3.60580	0.95623	0.19834	1.14157			
	N	4	6	4	4	5	1		
EOS	Mean	1.4453	0.9463	0.8470	1.0645	0.5228		(f)	(f)
(%E)	S.D.	1.46350	0.76445	0.40014	0.52747	0.14785			
	N	4	6	4	4	5	1		
BASO	Mean	1.0205	1.1072	0.8848	0.6000	0.8326		(f)	(f)
(%B)	S.D.	0.29894	0.19355	0.18311	0.45985	0.31047			
	N	4	6	4	4.00000	5	1		
RBC	Mean	8.330	8.388	8.263	8.615	8.026		(f)	(f)
(M/uL)	S.D.	0.6140	0.3534	0.2766	0.3569	0.3245			
	N	4	6	4	4	5	1		
HGB	Mean	15.15	15.00	15.25	15.43	14.34		(f)	(f)
(g/dL)	S.D.	1.261	0.559	0.265	0.624	0.378			
	N	4	6	4	4	5	1		
HCT	Mean	42.15	42.85	42.23	43.73	40.94		(f)	(f)
(%)	S.D.	2.728	1.915	1.144	1.374	1.496			
	N	4	6	4	4	5	1		
MCV	Mean	50.63	51.10	51.15	50.83	51.00		(f)	(f)
(fL)	S.D.	0.624	0.429	0.342	0.591	0.430			
	N	4	6	4	4	5	1		
MCH	Mean	18.78	19.07	18.73	18.50	18.72		(f)	(f)
(pg)	S.D.	0.457	0.838	0.532	0.658	0.835			
	N	4	6	4	4	5	1		
MCHC	Mean	37.05	37.37	36.65	36.40	36.76		(f)	(f)
(g/dL)	S.D.	0.387	1.565	1.038	0.891	1.488			
	N	4	6	4	4	5	1		
RDW	Mean	13.25	13.35	13.10	13.70	13.22		(f)	(f)
(%)	S.D.	0.526	0.423	0.183	0.730	0.303			
	N	4	6	4	4	5	1		
PLT	Mean	669.50	500.43	478.83	722.90	684.80		(f)	(f)
(K/uL)	S.D.	286.555	365.174	379.027	459.993	508.362			
	N	4	6	4	4	5	1		
MPV	Mean	10.613	9.735	9.503	9.660	9.290		(f)	(f)
(fL)	S.D.	2.4133	0.2125	0.4373	0.3351	0.3887			
	N	4	6	3	3	4	1		

= no data
(f) = All animals died on study

Table K-3
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

14-Day Individual Hematology
Male Rats

Group	Animal ID	WBC (K/uL)	NEU (%N)	LYM (%L)	MONO (%M)	EOS (%E)	BASO (%B)	RBC (M/uL)	HGB (g/dL)	HCT (%)	MCV (fL)	MCH (pg)	MCHC (g/dL)	RDW (%)	PLT (K/uL)	MPV (fL)
	04-185	7 16	15.700	82 100	0 168	0 687	1 370	8 40	14 3	41 9	49 9	17 7	35 4	14.1	790 0	9.84
Methylcellulose	04-186															
Control	04-192	1 69	8.820	89 700	0 492	0.197	0 754	6.89	12.0	35 1	50 9	18.6	36.5	12.8	23 4	
	04-194	9 63	14 300	83 400	0 229	0 940	1 100	8 95	14 2	44.0	49.1	17.7	36 1	14 3	404.0	9.47
	04-196	4 31	12.000	85 300	0 699	1 170	0.823	8 44	14.4	42.1	49.9	17 9	35 9	14 1	840 0	9 19
	04-221	8 40	13 700	81 500	2 840	0.733	1 140	8 73	15 2	43 6	49 9	18 1	36.3	14 5	847.0	10.20
	Mean	6.238	12.9040	84.4000	0.8856	0.7454	1.0374	8.282	14.02	41.34	49.94	18.00	36.04	13.96	580.88	9.675
	SD	3.2184	2.64085	3.30151	1.11305	0.36141	0.25067	0.3099	1.197	3.686	0.639	0.374	0.422	0.669	361.858	0.4397
	04-177	5 99	13 300	84 000	1 440	0 324	0 881	7.73	12 9	39 4	50 9	18 6	36 6	13 5	807.0	10 10
2.13 mg/kg	04-187	4 78	13 100	85 600	0 403	0 224	0 672	8.89	15.3	44 4	49 9	18 0	36 2	14 7	912 0	9.40
	04-200															
	04-209	5 51	12.300	78 500	6 920	0 888	1 460	8 19	13 7	41.8	51 0	18 4	36 0	13.6	169 0	9.25
	04-215	2 32	17 900	76 700	2 820	1 210	1.310	8 20	13 8	41.9	51.1	18.1	35 4	14 4	725 0	9.88
	04-217	8 20	15 100	83 200	0 210	0 832	0 643	9 00	15 0	44 8	49 8	17 8	35 8	14 8	88 9	11 40
	Mean	5.360	14.3400	81.6000	2.3586	0.6956	0.9932	8.402	14.14	42.46	50.54	18.18	36.00	14.20	560.38	10.006
	SD	2.1250	2.23786	3.80592	2.75245	0.41253	0.37305	0.5322	0.991	2.280	0.635	0.319	0.447	0.612	382.436	0.8525
	04-181	4 02	17 300	80 400	0 212	1 190	0 849	7 61	13 0	38 0	50 0	18 4	36 8	14.0	903.0	9 66
4.25 mg/kg	04-183	4 30	16 000	81 500	1 310	1 180	0 050	7 15	12.5	35 7	50.0	18 1	36 2	13 4	433.0	9.58
	04-205	6 45	12 700	86 100	0 246	0 378	0 606	8 05	13.5	41 1	51 0	18 4	36 1	12.8	45 9	
	04-208	8 31	14 600	83 800	0 173	0 399	0 997	8 38	13 6	42.2	50 3	17 3	34 4	14.5	894 0	10.40
	04-210	3 57	0.620	93 800	2 560	1 500	1 470	6 54	10.9	33 1	50.6	17.4	34.3	12.6	38 1	
	04-220	5 04	15 700	82 500	0 234	0 511	1 060	8 90	15 1	44.6	50 1	17 9	35 7	14 6	801 0	10 70
	Mean	5.282	12.8200	84.6833	0.7892	0.8597	0.8387	7.772	13.10	39.12	50.33	17.92	35.58	13.65	519.17	10.005
	SD	1.7933	6.17252	4.88156	0.97192	0.48735	0.47935	0.8544	1.387	4.304	0.398	0.479	1.019	0.853	407.453	0.5517
	04-173	4 80	16 800	80 700	0 924	0 654	0 947	8.31	14.7	41 6	50 1	18 1	36 1	15.0	954.0	10.80
8.50 mg/kg	04-174	5 06	11.100	85 800	1 560	0 577	0 897	8 92	15.4	45.0	50.4	18 1	35 9	14.8	917.0	9 54
	04-189															
	04-190	4 20	13 800	82 000	2 730	1 350	0 102	8 39	14 7	41.9	50.0	18 0	36.0	14 1	789 0	9.44
	04-199	5 69	9.910	88 100	0 190	0 815	0 985	8 32	14 3	41 7	50.1	17 9	35 7	13 8	829 0	9 55
	04-212	4 97	13 700	81 100	2 660	0 697	1 870	9 38	15 4	47 0	50 1	17 8	35.4	15 0	354 0	10 40
	Mean	4.944	13.0620	83.5400	1.6128	0.8186	0.9602	8.664	14.73	43.44	50.14	17.98	35.82	14.54	768.60	9.946
	SD	0.5358	2.67903	3.25161	1.10072	0.30929	0.62630	0.4735	0.596	2.444	0.152	0.130	0.277	0.555	241.015	0.6150
	04-179	9 13	10 200	87 700	0 786	0 749	0 604	8 79	15 3	43 9	50.0	17 6	35 3	14 8	940 0	9.37
17.00 mg/kg	04-193	2 54	11 500	85 100	1 850	0.595	0.948	7 48	12.5	38 1	51 0	18 2	35.7	13.0	85 7	8.44
	04-195	3 67	14 700	83 600	0 260	0 551	0 949	8 30	14.8	42.2	50 9	18 5	36.5	13 9	82 0	10.80
	04-201	7 23	15 000	82 200	1 750	0 403	0 687	7.58	12 5	39 0	51 5	18.5	35.9	13 3	900 0	10 70
	04-202	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-204	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	Mean	5.643	12.8500	84.6500	1.1615	0.5745	0.7970	8.038	13.78	40.80	50.85	18.20	35.85	13.75	581.93	9.828
	SD	3.0659	2.37276	2.35301	0.76900	0.14240	0.17819	0.6206	1.486	2.714	0.624	0.424	0.500	0.794	403.030	1.1316
	04-178	4 45	15 500	82 400	1 220	0 242	0 699	7 59	13 0	38 0	50.0	18 2	36 3	13.1	64 8	10 70
25.50 mg/kg	04-180	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-184	4 45	14.100	81 800	2 050	0 409	1 680	8.36	13.8	42.0	50.2	18.4	36 7	13.8	595 0	9 38
	04-207	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-213	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-219	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	Mean	4.450	14.8000	82.1000	1.6350	0.3255	1.1895	7.975	13.40	40.00	50.10	18.30	36.50	13.45	329.90	10.040
	SD	0.0000	0.98995	0.42426	0.58690	0.11809	0.69367	0.5445	0.566	2.828	0.141	0.141	0.283	0.495	374.900	0.9334
	04-175	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
34.00 mg/kg	04-182	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-191	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-198	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-203	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-206	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	Mean															
	SD															
	04-172	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
42.50 mg/kg	04-176	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-188	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-211	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-214	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-216	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	Mean															
	SD															

= no data
(f) = Animal died on study

Table K-4
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

14-Day Individual Hematology
Female Rats

Group	Animal ID	WBC (K/uL)	NEU (%N)	LYM (%L)	MONO (%M)	EOS (%E)	BASO (%B)	RBC (M/uL)	HGB (g/dL)	HCT (%)	MCV (fL)	MCH (pg)	MCHC (g/dL)	RDW (%)	PLT (K/uL)	MPV (fL)
	04-249															
Methylcellulose Control	04-253	1 25	72.000	12.400	11 100	3 630	0 973	8 95	16.5	44 6	49 8	18 2	36.6	13 7	904 0	9 42
	04-260															
	04-262	7 73	12 600	84 800	0 725	0 711	1 150	8 74	15.9	44 2	50 6	18 7	36 9	13.5	281.0	14.20
	04-272	5 13	11 700	84 700	2 450	0 545	0.629	7 97	14 4	40 9	51 3	19 3	37 5	13 3	866 0	9 81
	04-273	4 47	11.300	83 500	3 020	0 895	1 330	7 66	13.8	38 9	50 8	18 9	37.2	12 5	627 0	9 02
	Mean	**4.645**	**26.9000**	**66.3500**	**4.3238**	**1.4453**	**1.0205**	**8.330**	**15.15**	**42.15**	**50.63**	**18.78**	**37.05**	**13.25**	**669.50**	**10.613**
	SD	**2.6652**	**30.07158**	**35.97152**	**4.62166**	**1.46350**	**0.29894**	**0.6148**	**1.261**	**2.728**	**0.624**	**0.457**	**0.387**	**0.526**	**286.555**	**2.4133**
	04-237	6.71	16.500	79 900	1 330	0.925	1.300	8 40	14 8	42 4	50 5	17.7	35.1	13 5	711 0	9 95
2.13 mg/kg	04-241	8.19	8 840	89.200	0 329	0 789	0.803	8 15	14 1	41 9	51 4	19.0	37 1	13 2	71 6	
	04-247	8 30	11 000	86 800	0 652	0 426	1 090	8 84	15 7	45 7	51.7	18 8	36 4	14 0	889 0	9 63
	04-274	4 99	14 300	83 600	0 801	0.350	0.970	8 71	15 3	44 4	51 0	19 6	38 4	13 3	150 0	9 87
	04-279	3.62	11.300	85 700	1 020	0 748	1.200	8 35	15 3	42.4	50 8	19 1	37 6	13 4	318 0	
	04-281	0 43	74.600	12 100	9 620	2.440	1 280	7.88	14 8	40 3	51 2	20 2	39 6	12 7	863 0	9.49
	Mean	**5.374**	**22.7567**	**72.8833**	**2.2928**	**0.9463**	**1.1071**	**8.388**	**15.00**	**42.85**	**51.10**	**19.07**	**37.37**	**13.35**	**500.43**	**9.735**
	SD	**3.0303**	**25.54032**	**29.94284**	**3.60580**	**0.76445**	**0.19355**	**0.3534**	**0.559**	**1.915**	**0.429**	**0.838**	**1.565**	**0.423**	**365.174**	**0.2125**
	04-239	5 61	16 000	81 400	0 909	0 697	0 987	8 15	15 1	41.8	51.3	19.0	37 1	12 9	693.0	9.72
4.25 mg/kg	04-243															
	04-244															
	04-268	3 05	9.400	89 100	0 219	0 494	0 750	8.27	15.3	42.2	51.1	19.3	37 9	13 2	71 3	
	04-269	5 58	10 100	85.000	2 360	1 420	1.090	8.64	15.6	43.8	50 7	18.1	35 7	13 3	259 0	9 00
	04-271	4 95	14 100	83 900	0 475	0 777	0 712	7 99	15 0	41 1	51 5	18 5	35 9	13 0	892 0	9 79
	Mean	**4.798**	**12.4000**	**84.8500**	**0.9908**	**0.8470**	**0.8848**	**8.263**	**15.25**	**42.23**	**51.15**	**18.73**	**36.65**	**13.10**	**478.83**	**9.503**
	SD	**1.2841**	**3.16965**	**3.28884**	**0.95623**	**0.40014**	**0.18311**	**0.2766**	**0.265**	**1.144**	**0.342**	**0.532**	**1.038**	**0.183**	**379.027**	**0.4373**
	04-233															
8.50 mg/kg	04-234															
	04-242	4 15	17 600	80 500	0.545	0 990	0 347	8 58	15 6	43 9	51.2	18 9	36.9	14.5	976 0	9 33
	04-246	4 12	16.800	81 100	0.548	0.418	1 150	8.36	15.8	42.8	51.3	19 2	37.4	13.3	956 0	10.00
	04-259	5 24	15.900	82 100	0.149	1 700	0.117	8 39	14 5	42.6	50.8	18 1	35.6	12 9	33 6	
	04-263	5 40	10 600	87 000	0.544	1.150	0.786	9 13	15 8	45.6	50 0	17 8	35.7	14 1	926 0	9 65
	Mean	**4.778**	**15.2250**	**82.6750**	**0.4465**	**1.0645**	**0.6000**	**8.615**	**15.43**	**43.73**	**50.83**	**18.50**	**36.40**	**13.70**	**722.90**	**9.660**
	SD	**0.6368**	**3.16856**	**2.95790**	**0.19834**	**0.52747**	**0.45985**	**0.3569**	**0.624**	**1.374**	**0.591**	**0.658**	**0.891**	**0.730**	**459.993**	**0.3351**
	04-238	6 59	9.570	89 100	0 196	0.310	0 783	8.03	13 8	41 4	51 6	18 5	35 9	12 8	203 0	9 64
17.00 mg/kg	04-248	5 50	12 000	85 900	0 314	0 668	1 100	8 18	14.7	41 6	50 8	18 3	36 1	13 2	898 0	9 20
	04-252															
	04-256	7 16	13.600	84 800	1 980	0 639	0 989	8.11	14 3	41 0	50 6	18 2	36 0	13 6	910 0	8 78
	04-264	3 76	9.510	88 700	0 285	0 555	0.975	8 33	14 7	42 3	50.7	18 4	36 4	13 4	113 0	
	04-275	5 13	20 900	75 700	2 630	0 442	0 316	7 48	14 2	38 4	51 3	20.2	39 4	13 1	1300 0	9 54
	Mean	**5.628**	**12.7160**	**84.8400**	**1.8010**	**0.5228**	**0.8326**	**8.026**	**14.34**	**40.94**	**51.00**	**18.72**	**36.76**	**13.22**	**684.80**	**9.290**
	SD	**1.3254**	**4.71465**	**5.42476**	**1.14157**	**0.14785**	**0.31047**	**0.3245**	**0.378**	**1.496**	**0.430**	**0.835**	**1.488**	**0.303**	**508.362**	**0.3887**
	04-240	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
25.50 mg/kg	04-261	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-266	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-270															
	04-276	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-280	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	Mean															
	SD															
	04-232	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
34.00 mg/kg	04-250	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-251	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-257	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-258	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-277	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	Mean															
	SD															
	04-236	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
42.50 mg/kg	04-245	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-254	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-255	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-265	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	04-267	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	Mean															
	SD															

= no data
(f) = Animal died on study

APPENDIX L

SUMMARY OF 90-DAY CLINICAL OBSERVATIONS

Table L-1
Subchronic Oral Toxicity of RDX in Rats

Summary of 90-Day Clinical Observations
Male Rats

Observation (n=10)	Number of Animals Dose Groups (mg/kg)					
	Methylcellulose Control	4	8	10	12	15
Arousal						
Low (some movement)				1		
High				5	4	10
Very High				1	1	2
Eyes						
Crusty Eyes	5	4	5	7	6	6
Blepharosis				1		
Gastrointestinal Signs						
Diarrhea		2				
Salivation					1	
Hemorrhage						
Hemorrhage				2		1
Integumentary Signs						
Abrasion						4
Barbering	1	2	4	7	5	5
Rough Haircoat				2		6
Stained Haircoat				1		1
Dried Red Material				1		6
Neuromuscular Signs						
Convulsions			1	3	8	7
Tremors					2	3
Respiration						
Congested Breathing			1			1
Mortality						
Found Dead			1	3	2	3

Table L-2
Subchronic Oral Toxicity of RDX in Rats

Summary of 90-Day Clinical Observations
Female Rats

Observation (n=10)	Number of Animals Female Dose Groups (mg/kg)					
	Methylcellulose Control	4	8	10	12	15
Arousal						
High			1		4	8
Very High						1
Eyes						
Crusty Eyes	9	10	10	9	8	8
Hemorrhage						
Hemorrhage				1		1
Integumentary Signs						
Barbering	2	3	3	5	3	7
Rough Haircoat						1
Stained Haircoat						2
Dried Red Material			1	2		3
Neuromuscular Signs						
Convulsions			2	3	5	5
Tremors						1
Gait						
Hindlimb Impairment		1				
Mortality						
Found Dead			1	2	5	4

APPENDIX M

90-DAY INDIVIDUAL URINALYSIS DATA

Table M-1
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Urinalysis Data
Male Rats
19 Jan - 21 Jan 2005

Group	Animal #	Volume (ml)	Color	Appearance	Glucose	Bilirubin	Ketone (g/L)	Specific Gravity	Blood (ery/uL)	pH	Protein (mg/dL)	Urobilinogen (mg/dL)	Nitrite	Leukocytes (leuko/uL)
Methylcellulose Control	05-011	3.0	dk. yellow	cloudy	neg.	neg.	neg.	1.035	neg.	7.0	300	0.2	neg.	neg.
	05-012	6.0	straw	clear	neg.	neg.	neg.	1.028	neg.	7.0	100	0.2	neg.	trace
	05-016	9.0	straw	sl. cloudy	neg.	neg.	neg.	1.021	hem. trace	8.0	100	0.2	neg.	neg.
	05-020	4.0	yellow	clear	neg.	neg.	neg.	1.033	neg.	7.0	30	0.2	neg.	neg.
	05-023	10.0	yellow	cloudy	neg.	neg.	neg.	1.026	hem. trace	7.5	30	0.2	neg.	neg.
	05-052	7.0	yellow	clear	neg.	neg.	neg.	1.029	neg.	7.5	30	0.2	neg.	neg.
	05-060	8.0	yellow	sl. cloudy	neg.	neg.	neg.	1.028	neg.	7.0	30	0.2	neg.	neg.
	05-064	13.0	straw	clear	neg.	neg.	neg.	1.020	neg.	7.5	30	0.2	neg.	neg.
	Mean	**7.50**						**1.0275**		**7.31**	**81.3**	**0.20**		
	SD	**3.251**						**0.00521**		**0.372**	**93.87**	**0**		
4 mg/kg	05-001	4.0	dk. yellow	sl. cloudy	neg.	neg.	neg.	1.035	neg.	7.0	100	0.2	neg.	neg.
	05-007	6.0	yellow	sl. cloudy	neg.	neg.	neg.	1.030	neg.	8.0	30	0.2	neg.	neg.
	05-013	4.0	dk. yellow	sl. cloudy	neg.	neg.	neg.	1.035	neg.	7.5	30	0.2	neg.	neg.
	05-028	3.0	yellow	sl. cloudy	neg.	neg.	neg.	1.035	neg.	7.0	100	0.2	neg.	neg.
	05-033	5.0	yellow	sl. cloudy	neg.	neg.	neg.	1.027	neg.	7.5	30	0.2	neg.	neg.
	05-039	2.0	dk. yellow	sl. cloudy	neg.	neg.	neg.	1.035	neg.	6.5	100	0.2	neg.	neg.
	05-041	6.0	yellow	sl. cloudy	neg.	neg.	neg.	1.028	neg.	8.0	30	0.2	neg.	neg.
	05-055	4.0	dk. yellow	sl. cloudy	neg.	neg.	neg.	1.035	neg.	7.0	30	0.2	neg.	neg.
	Mean	**4.25**						**1.0325**		**7.31**	**56.3**	**0.20**		
	SD	**1.389**						**0.00355**		**0.530**	**36.23**	**0**		
8 mg/kg	05-003	3.0	yellow	sl. cloudy	neg.	neg.	neg.	1.035	neg.	7.0	100	0.2	neg.	neg.
	05-006	3.5	yellow	cloudy	neg.	neg.	neg.	1.035	neg.	7.5	100	0.2	neg.	neg.
	05-015	5.0	straw	sl. cloudy	neg.	neg.	neg.	1.025	neg.	7.5	30	0.2	neg.	neg.
	05-034	6.5	straw	sl. cloudy	neg.	neg.	neg.	1.023	neg.	7.0	30	0.2	neg.	neg.
	05-037	4.5	straw	sl. cloudy	neg.	neg.	neg.	1.035	neg.	7.0	100	0.2	neg.	neg.
	05-046	9.5	straw	sl. cloudy	neg.	neg.	neg.	1.019	neg.	8.0	trace	0.2	neg.	neg.
	05-051	3.5	straw	sl. cloudy	neg.	neg.	neg.	1.035	hem. trace	7.5	300	0.2	neg.	neg.
	05-068	6.5	straw	sl. cloudy	neg.	neg.	neg.	1.024	neg.	7.5	100	0.2	neg.	neg.
	Mean	**5.25**						**1.0289**		**7.38**	**108.6**	**0.20**		
	SD	**2.171**						**0.00677**		**0.354**	**90.63**	**0**		
10 mg/kg	05-024	2.5	yellow	sl. cloudy	neg.	neg.	neg.	1.035	neg.	7.0	100	0.2	neg.	neg.
	05-040	12.5	yellow	sl. cloudy	neg.	neg.	neg.	1.021	neg.	8.0	30	0.2	neg.	neg.
	05-042	11.0	straw	sl. cloudy	neg.	neg.	neg.	1.023	neg.	7.5	30	0.2	neg.	neg.
	05-049	8.0	straw	sl. cloudy	neg.	neg.	neg.	1.020	neg.	7.5	100	0.2	neg.	neg.
	05-050	11.0	straw	sl. cloudy	neg.	neg.	neg.	1.016	neg.	8.0	trace	0.2	neg.	neg.
	05-053	5.5	straw	sl. cloudy	neg.	neg.	neg.	1.029	neg.	7.0	30	0.2	neg.	neg.
	05-054	0.0	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
	05-065	15.0	straw	cloudy	neg.	neg.	neg.	1.017	neg.	8.0	30	1	pos.	neg.
	Mean	**8.19**						**1.0230**		**7.57**	**53.3**	**0.31**		
	SD	**5.175**						**0.00681**		**0.450**	**36.15**	**0.302**		
12 mg/kg	05-005	3.5	straw	sl. cloudy	neg.	neg.	neg.	1.035	neg.	7.0	100	0.2	neg.	neg.
	05-009	2.5	yellow	cloudy	neg.	neg.	trace	1.035	neg.	8.5	100	0.2	neg.	neg.
	05-021	9.5	straw	sl. cloudy	neg.	neg.	neg.	1.024	neg.	8.0	trace	0.2	neg.	neg.
	05-027	4.0	straw	sl. cloudy	neg.	neg.	neg.	1.035	neg.	7.0	100	0.2	neg.	trace
	05-031	11.0	straw	sl. cloudy	neg.	neg.	neg.	1.015	hem. trace	8.0	trace	0.2	pos.	neg.
	05-047	14.0	straw	sl. cloudy	neg.	neg.	neg.	1.020	neg.	7.5	30	0.2	neg.	neg.
	05-048	4.0	yellow	sl. cloudy	neg.	neg.	neg.	1.035	hem. trace	6.5	100	0.2	neg.	neg.
	05-063	22.0	straw	sl. cloudy	neg.	neg.	neg.	1.013	neg.	8.5	trace	0.2	neg.	neg.
	Mean	**8.81**						**1.0265**		**7.63**	**86.0**	**0.20**		
	SD	**6.766**						**0.00965**		**0.744**	**31.30**	**0**		
15 mg/kg	05-018	3.0	straw	sl. cloudy	neg.	neg.	neg.	1.035	neg.	6.5	100	0.2	neg.	neg.
	05-022	3.0	yellow	sl. cloudy	neg.	neg.	neg.	1.035	neg.	7.0	100	0.2	neg.	trace
	05-030	3.0	straw	sl. cloudy	neg.	neg.	neg.	1.035	neg.	6.5	30	0.2	neg.	neg.
	05-032	7.5	straw	sl. cloudy	neg.	neg.	neg.	1.029	neg.	7.0	30	0.2	neg.	neg.
	05-035	5.5	yellow	sl. cloudy	neg.	neg.	neg.	1.035	neg.	7.0	100	0.2	neg.	neg.
	05-043	9.5	straw	sl. cloudy	neg.	neg.	neg.	1.029	neg.	7.5	30	0.2	neg.	neg.
	05-057	5.5	straw	sl. cloudy	neg.	neg.	neg.	1.035	neg.	6.5	100	0.2	neg.	neg.
	Mean	**5.29**						**1.0333**		**6.86**	**70.0**	**0.20**		
	SD	**2.531**						**0.00293**		**0.378**	**37.42**	**0**		

sl: slightly
dk: dark
pos: positive
neg: negative
hem. hemolyzed

Table M-2
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Urinalysis Data
Female Rats
04 Feb - 05 Feb 2005

Group	Animal #	Volume (ml)	Color	Appearance	Glucose	Bilirubin	Ketone (g/L)	Specific Gravity	Blood (ery/uL)	pH	Protein (mg/dL)	Urobilinogen (mg/dL)	Nitrite	Leukocytes (leuko/uL)
Methylcellulose Control	05-076	5.0	yellow	sl. cloudy	neg.	neg.	neg.	1.030	neg.	6.5	trace	0.2	neg.	neg.
	05-077	4.5	yellow	clear	neg.	neg.	neg.	1.031	neg.	6.5	trace	0.2	neg.	neg.
	05-084	10.5	straw	clear	neg.	neg.	neg.	1.011	small	7.0	trace	0.2	neg.	neg.
	05-088	5.0	straw	sl. cloudy	neg.	neg.	neg.	1.026	neg.	7.0	trace	0.2	neg.	neg.
	05-098	7.0	straw	sl. cloudy	neg.	neg.	neg.	1.018	neg.	7.5	neg.	0.2	neg.	neg.
	05-100	4.0	straw	clear	neg.	neg.	neg.	1.035	neg.	6.5	trace	0.2	neg.	neg.
	05-101	0.5	straw	clear	neg.	neg.	neg.	1.035	neg.	6.0	30	0.2	pos.	neg.
	05-114	4.5	straw	clear	neg.	neg.	neg.	1.029	neg.	7.0	trace	0.2	neg.	neg.
	Mean	**5.13**						**1.0269**		**6.75**	**30.0**	**0.20**		
	SD	**2.825**						**0.00841**		**0.463**		**0**		
4 mg/kg	05-072	4.0	straw	clear	neg.	neg.	neg.	1.023	neg.	7.0	trace	0.2	neg.	neg.
	05-078	9.5	straw	clear	neg.	neg.	neg.	1.015	neg.	7.0	neg.	0.2	neg.	neg.
	05-081	4.0	straw	clear	neg.	neg.	neg.	1.032	non-hem. trace	7.0	trace	0.2	neg.	neg.
	05-090	3.0	straw	sl. cloudy	neg.	neg.	neg.	1.028	non-hem. mod.	7.0	trace	0.2	neg.	neg.
	05-094	9.0	straw	clear	neg.	neg.	neg.	1.015	neg.	7.0	neg.	0.2	pos.	neg.
	05-095	4.5	straw	sl. cloudy	neg.	neg.	neg.	1.026	neg.	7.0	trace	0.2	pos.	neg.
	05-105	4.5	straw	clear	neg.	neg.	neg.	1.030	neg.	6.5	neg.	0.2	neg.	neg.
	05-115	2.0	straw	clear	neg.	neg.	neg.	1.029	neg.	7.0	trace	0.2	neg.	neg.
	Mean	**5.06**						**1.0248**		**6.94**		**0.20**		
	SD	**2.718**						**0.00658**		**0.177**		**0**		
8 mg/kg	05-071	2.5	yellow	clear	neg.	neg.	neg.	1.035	hem. trace	7.0	30	0.2	neg.	neg.
	05-074	7.5	straw	sl. cloudy	neg.	neg.	neg.	1.022	neg.	7.0	trace	0.2	neg.	neg.
	05-075	3.5	straw	clear	neg.	neg.	neg.	1.034	neg.	6.5	trace	0.2	neg.	neg.
	05-085	8.5	straw	clear	neg.	neg.	neg.	1.017	non-hem. Trace	7.0	trace	0.2	neg.	neg.
	05-086	8.5	straw	clear	neg.	neg.	neg.	1.025	neg.	6.5	trace	0.2	neg.	neg.
	05-102	6.5	straw	sl. cloudy	neg.	neg.	neg.	1.024	neg.	7.0	trace	0.2	neg.	neg.
	05-106	7.5	straw	clear	neg.	neg.	neg.	1.020	hem. trace	7.0	trace	0.2	pos.	neg.
	05-108	17.0	straw	clear	neg.	neg.	neg.	1.010	neg.	6.5	trace	0.2	neg.	neg.
	Mean	**7.69**						**1.0234**		**6.81**	**30.0**	**0.20**		
	SD	**4.375**						**0.00831**		**0.259**		**0**		
10 mg/kg	05-073	17.0	straw	clear	neg.	neg.	neg.	1.010	neg.	7.0	neg.	0.2	neg.	neg.
	05-083	5.0	straw	clear	neg.	neg.	neg.	1.021	neg.	7.0	trace	0.2	neg.	neg.
	05-109	6.0	straw	clear	neg.	neg.	neg.	1.023	neg.	7.0	trace	0.2	pos.	neg.
	05-110	5.0	yellow	clear	neg.	neg.	neg.	1.030	neg.	7.0	30	0.2	neg.	neg.
	05-117	5.5	straw	sl. cloudy	neg.	neg.	neg.	1.027	neg.	6.5	30	0.2	neg.	neg.
	05-130	13.0	straw	clear	neg.	neg.	neg.	1.016	neg.	7.0	trace	0.2	neg.	neg.
	05-131	11.0	straw	clear	neg.	neg.	neg.	1.016	neg.	7.5	trace	0.2	pos.	neg.
	05-132	3.0	straw	clear	neg.	neg.	neg.	1.035	neg.	6.5	30	0.2	neg.	neg.
	Mean	**8.19**						**1.0223**		**6.94**	**30.0**	**0.20**		
	SD	**4.899**						**0.00824**		**0.320**	**0**	**0**		
12 mg/kg	05-082	18.0	straw	clear	neg.	neg.	neg.	1.014	neg.	7.0	trace	0.2	neg.	neg.
	05-087	18.0	straw	clear	neg.	neg.	neg.	1.012	neg.	7.0	neg.	0.2	pos.	neg.
	05-121	15.0	straw	clear	neg.	neg.	neg.	1.013	neg.	7.5	trace	0.2	neg.	neg.
	05-124	20.0	straw	clear	neg.	neg.	neg.	1.011	neg.	7.5	trace	0.2	pos.	neg.
	05-134	18.0	straw	clear	neg.	neg.	neg.	1.011	neg.	7.5	trace	0.2	neg.	neg.
	Mean	**17.80***						**1.0122**		**7.30**		**0.20**		
	SD	**1.789**						**0.00130**		**0.274**		**0**		
15 mg/kg	05-097	20.0	straw	clear	neg.	neg.	neg.	1.013	neg.	7.5	trace	0.2	pos.	neg.
	05-104	30.0	straw	clear	neg.	neg.	neg.	1.009	neg.	7.0	neg.	0.2	neg.	neg.
	05-107	18.0	straw	clear	neg.	neg.	neg.	1.014	neg.	7.5	trace	0.2	neg.	neg.
	05-113	5.0	yellow	clear	neg.	neg.	neg.	1.035	neg.	6.5	trace	0.2	neg.	neg.
	05-116	28.0	straw	clear	neg.	neg.	neg.	1.007	neg.	7.0	neg.	0.2	pos.	neg.
	05-133	5.0	yellow	clear	neg.	neg.	neg.	1.035	neg.	7.0	30	0.2	pos.	neg.
	Mean	**17.67***						**1.0188**		**7.08**	**30.0**	**0.20**		
	SD	**10.820**						**0.01278**		**0.376**		**0**		

sl: slightly
dk: dark
pos: positive
neg: negative
hem: hemolyzed
* p less than or equal to 0.05
ANOVA with Holm-Sidak Method

APPENDIX N

SUMMARY OF 90-DAY BODY WEIGHTS AND INDIVIDUAL BODY WEIGHT DATA

Appendix N
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Summary of 90-Day Body Weights

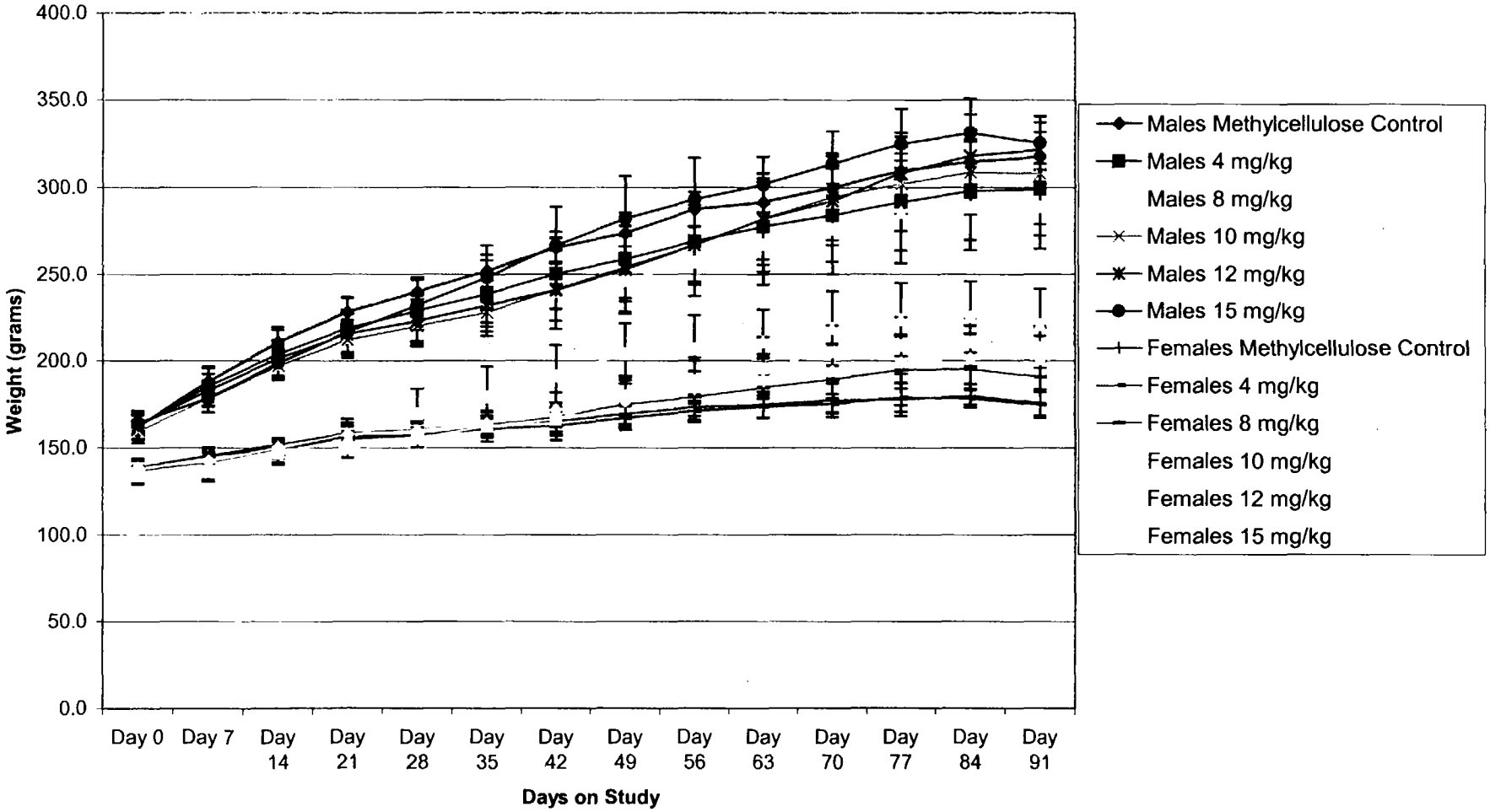


Table N-1
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Summary of Body Weights (grams)
Male Rats

Period		Methylcellulose Control	RDX in 1% Methylcellulose / 0.2% Tween 80				
			4 mg/kg	8 mg/kg	10 mg/kg	12 mg/kg	15 mg/kg
Day 0	Mean	162.0	162.3	163.6	159.4	162.8	164.2
	S.D.	6.70	7.72	6.43	6.62	8.30	6.25
	N	10	10	10	10	10	10
Day 7	Mean	188.1	185.6	179.8	178.2	183.0	178.6
	S.D.	7.52	11.01	5.55	8.05	9.42	8.19
	N	10	10	10	10	10	10
Day 14	Mean	210.8	204.1	197.9*	197.0*	201.6	198.8*
	S.D.	8.44	13.63	8.31	6.94	10.35	10.02
	N	10	10	10	10	10	10
Day 21	Mean	228.2	218.9	213.3*	212.0*	215.7	216.8
	S.D.	8.43	17.23	10.25	7.20	11.40	12.70
	N	10	10	10	10	10	10
Day 28	Mean	239.9	229.0	222.2*	220.0*	223.1*	232.3
	S.D.	8.33	18.51	13.31	8.72	14.95	14.46
	N	10	10	10	10	9	10
Day 35	Mean	252.0	238.8	231.7*	228.0*	232.3*	248.3
	S.D.	9.29	19.25	14.94	6.18	18.21	18.24
	N	10	10	10	9	9	10
Day 42	Mean	265.3	250.4	240.1*	241.3*	241.0*	266.5
	S.D.	9.15	20.55	17.19	11.60	22.76	22.29
	N	10	10	10	9	9	10
Day 49	Mean	273.7	258.7	246.5*	254.2	253.0	282.1
	S.D.	11.50	24.54	19.47	18.08	24.91	24.28
	N	10	10	10	9	9	10
Day 56	Mean	287.4	269.1	257.2*	266.7	266.8	293.1
	S.D.	9.91	24.32	20.03	21.10	23.03	23.78
	N	10	10	10	9	9	9
Day 63	Mean	291.4	277.4	267.3	281.9	281.8	301.6
	S.D.	16.76	25.84	23.32	23.30	26.18	15.95
	N	10	10	10	9	9	9
Day 70	Mean	300.0	284.1	276.1	294.6	292.3	313.5
	S.D.	12.67	26.80	26.03	24.89	25.62	18.64
	N	10	10	10	9	8	8
Day 77	Mean	309.4	291.5	285.9	302.0	308.1	324.8
	S.D.	13.84	27.91	29.47	27.09	23.28	20.10
	N	10	10	10	8	8	8
Day 84	Mean	314.6	298.0	288.8	308.6	318.0	331.4
	S.D.	13.00	28.30	25.01	24.30	23.72	19.62
	N	10	10	9	8	8	8
Day 91	Mean	317.5	299.1	289.2*	308.0	321.6	325.4
	S.D.	14.14	26.76	24.50	29.26	19.33	15.16
	N	10	10	9	7	8	7

* p less than or equal to 0.05
ANOVA with Holm-Sidak Method

Table N-2
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Summary of Body Weights (grams)
Female Rats

Period		Methylcellulose Control	RDX in 1% Methylcellulose / 0.2% Tween 80				
			4 mg/kg	8 mg/kg	10 mg/kg	12 mg/kg	15 mg/kg
Day 0	Mean	138.7	138.9	136.9	138.4	133.9	134.8
	S.D.	3.97	4.86	5.45	4.95	4.89	4.85
	N	10	10	10	10	10	10
Day 7	Mean	145.7	145.2	141.6	142.4	136.4*	137.2*
	S.D.	3.62	5.12	6.11	4.65	5.85	5.43
	N	10	10	10	10	10	10
Day 14	Mean	151.9	150.0	149.4	150.0	147.3	147.0
	S.D.	3.60	5.12	5.74	4.35	5.83	6.72
	N	10	10	10	10	9	8
Day 21	Mean	158.4	156.1	154.9	157.7	149.5	155.3
	S.D.	4.35	5.93	4.54	6.46	2.66	11.00
	N	10	10	9	9	6	8
Day 28	Mean	160.2	157.2	157.0	159.7	155.2	169.5
	S.D.	5.41	6.88	4.74	6.46	3.06	14.36
	N	10	10	9	9	6	8
Day 35	Mean	163.7	160.6	162.1	163.9	162.2	179.1*
	S.D.	6.53	7.11	6.19	7.30	4.45	17.38
	N	10	10	9	9	6	8
Day 42	Mean	165.1	162.5	167.6	171.8	166.2	191.3*
	S.D.	7.34	8.14	8.40	9.91	9.41	17.65
	N	10	10	9	9	6	8
Day 49	Mean	169.3	167.0	174.7	176.8	179.8	204.0*
	S.D.	7.39	6.85	13.98	13.33	11.30	17.43
	N	10	10	9	9	6	7
Day 56	Mean	173.1	171.0	179.1	183.9	188.4	206.6*
	S.D.	7.34	5.79	14.78	15.92	13.24	19.52
	N	10	10	9	9	5	7
Day 63	Mean	174.6	173.5	184.4	188.7	195.8	211.0*
	S.D.	7.56	6.59	17.16	15.05	17.70	18.48
	N	10	10	9	9	5	7
Day 70	Mean	177.2	175.2	189.3	194.2	205.0*	218.7*
	S.D.	9.82	5.53	19.09	15.85	15.15	21.44
	N	10	10	9	9	5	6
Day 77	Mean	177.6	178.7	194.6*	199.0*	208.8*	223.8*
	S.D.	9.56	8.11	20.28	15.19	16.24	21.17
	N	10	10	9	8	5	6
Day 84	Mean	179.6	178.2	195.1	201.5	210.6*	225.3*
	S.D.	6.74	5.27	20.63	18.56	13.87	20.53
	N	10	10	9	8	5	6
Day 90	Mean	175.6	174.7	190.6	200.9*	207.8*	220.8*
	S.D.	7.38	7.10	23.51	17.46	12.05	20.70
	N	10	10	9	8	5	6

* p less than or equal to 0.05
ANOVA with Holm-Sidak Method

Table N-3
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

90-Day Individual Body Weights (grams)
Male Rats

	Animal ID	Day 0	Day 7	Day 14	Day 21	Day 28	Day 35	Day 42	Day 49	Day 56	Day 63	Day 70	Day 77	Day 84	Day 91
Methylcellulose	05-011	168	194	224	240	256	269	280	289	304	309	318	330	331	341
Control	05-012	166	194	217	231	246	259	273	281	293	302	308	320	322	323
	05-016	163	193	215	234	246	259	274	284	293	298	301	307	314	316
	05-020	164	194	219	239	244	257	264	259	285	254	288	295	303	311
	05-023	160	185	209	230	239	251	267	278	293	300	305	313	317	319
	05-052	157	181	203	218	229	237	249	255	269	272	276	284	288	290
	05-060	153	178	201	219	233	245	260	277	287	299	311	322	330	334
	05-064	151	179	203	222	237	250	262	273	281	287	290	306	311	307
	05-066	166	184	201	218	230	243	256	261	277	290	295	300	308	313
	05-070	172	199	216	231	239	250	268	280	292	303	308	317	322	321
	Mean	**162.0**	**188.1**	**210.8**	**228.2**	**239.9**	**252.0**	**265.3**	**273.7**	**287.4**	**291.4**	**300.0**	**309.4**	**314.6**	**317.5**
	SD	**6.70**	**7.52**	**8.44**	**8.43**	**8.33**	**9.29**	**9.15**	**11.50**	**9.91**	**16.76**	**12.67**	**13.84**	**13.00**	**14.14**
4 mg/kg	05-001	166	187	200	217	225	241	258	259	272	281	288	292	296	300
	05-007	176	204	219	237	251	259	260	291	302	313	318	327	336	336
	05-013	160	176	190	197	206	213	221	222	232	238	242	248	254	256
	05-028	171	198	219	231	235	243	260	269	281	285	294	301	305	300
	05-033	159	183	196	199	213	222	234	241	251	258	266	275	281	281
	05-039	155	184	203	223	234	248	259	268	278	288	297	307	310	310
	05-041	165	187	210	226	241	248	264	269	280	289	296	304	311	316
	05-055	164	190	214	237	248	260	274	283	290	303	311	320	327	326
	05-062	157	183	213	231	241	250	262	268	277	284	290	297	309	308
	05-067	150	164	177	191	196	204	212	217	228	235	239	244	251	258
	Mean	**162.3**	**185.6**	**204.1**	**218.9**	**229.0**	**238.8**	**250.4**	**258.7**	**269.1**	**277.4**	**284.1**	**291.5**	**298.0**	**299.1**
	SD	**7.72**	**11.01**	**13.63**	**17.23**	**18.51**	**19.25**	**20.55**	**24.54**	**24.32**	**25.84**	**26.80**	**27.91**	**28.30**	**26.76**
8 mg/kg	05-003	157	170	178	191	194	201	205	209	221	224	235	240	251	253
	05-006	168	180	198	215	220	224	232	239	247	254	264	269	275	288
	05-015	171	183	196	205	206	215	222	222	229	235	238	246	256	251
	05-034	157	177	193	207	219	232	241	241	265	277	293	311	321	314
	05-037	165	183	203	221	231	243	247	254	265	277	285	292	303	297
	05-045	171	184	206	225	233	247	256	257	268	292	312	331	(f)	(f)
	05-046	167	187	205	220	234	243	253	267	284	291	302	310	315	320
	05-051	166	182	204	223	235	246	262	271	277	287	293	304	306	308
	05-068	162	181	201	214	227	237	248	258	263	273	277	285	292	290
	05-069	152	171	195	212	223	229	235	247	253	263	262	271	280	282
	Mean	**163.6**	**179.8**	**197.9**	**213.3**	**222.2**	**231.7**	**240.1**	**246.5**	**257.2**	**267.3**	**276.1**	**285.9**	**288.8**	**289.2**
	SD	**6.43**	**5.55**	**8.31**	**10.25**	**13.31**	**14.94**	**17.19**	**19.47**	**20.03**	**23.32**	**26.03**	**29.47**	**25.01**	**24.50**
10 mg/kg	05-017	151	171	192	209	212	225	245	272	293	306	302	(f)	(f)	(f)
	05-024	149	162	186	201	210	225	235	241	249	261	269	270	276	255
	05-040	165	186	202	215	219	224	234	251	268	282	303	309	322	333
	05-042	171	184	204	220	226	236	253	274	285	308	320	335	336	336
	05-049	161	172	187	203	212	223	230	233	239	254	268	277	288	294
	05-050	156	177	199	216	229	241	246	250	258	267	275	282	293	296
	05-053	164	183	197	209	217	225	230	234	244	260	274	284	291	310
	05-054	162	188	207	224	238	227	264	283	296	316	339	337	339	(f)
	05-056	157	182	200	214	218	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-065	158	177	196	209	219	226	235	250	268	283	301	322	324	332
	Mean	**159.4**	**178.2**	**197.0**	**212.0**	**220.0**	**228.0**	**241.3**	**254.2**	**266.7**	**281.9**	**294.6**	**302.0**	**308.6**	**308.0**
	SD	**6.62**	**8.05**	**6.94**	**7.20**	**8.72**	**6.18**	**11.60**	**18.08**	**21.10**	**23.30**	**24.89**	**27.09**	**24.30**	**29.26**
12 mg/kg	05-005	145	165	182	196	204	217	225	248	258	278	296	319	328	326
	05-009	155	176	190	204	210	212	217	226	245	252	266	275	282	290
	05-019	167	191	210	220	241	258	275	278	292	315	(f)	(f)	(f)	(f)
	05-021	173	194	213	230	236	245	249	259	275	285	303	318	333	327
	05-027	170	193	209	225	231	235	244	261	267	281	299	310	320	330
	05-031	166	180	195	206	206	212	214	224	244	256	264	287	298	306
	05-047	161	174	195	207	211	216	221	221	234	248	262	286	295	306
	05-048	168	184	207	224	233	246	256	271	290	308	325	342	348	342
	05-058	158	183	206	221	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-063	165	190	209	224	236	250	268	289	296	313	323	328	340	346
	Mean	**162.8**	**183.0**	**201.6**	**215.7**	**223.1**	**232.3**	**241.0**	**253.0**	**266.8**	**281.8**	**292.3**	**308.1**	**318.0**	**321.6**
	SD	**8.30**	**9.42**	**10.35**	**11.40**	**14.95**	**18.21**	**22.76**	**24.91**	**23.03**	**26.18**	**25.62**	**23.28**	**23.72**	**19.33**
15 mg/kg	05-008	171	182	209	240	257	279	304	322	337	316	(f)	(f)	(f)	(f)
	05-010	160	184	201	213	226	245	254	278	295	300	318	323	331	(f)
	05-018	161	167	181	192	212	220	237	244	258	285	297	304	309	304
	05-022	168	184	206	219	239	257	273	285	301	301	314	319	326	318
	05-025	167	187	202	223	247	267	292	311	(f)	(f)	(f)	(f)	(f)	(f)
	05-030	160	168	189	207	223	244	263	274	290	294	303	318	322	323
	05-032	172	182	200	219	225	233	255	266	277	291	302	308	315	315
	05-035	162	181	199	222	223	238	248	268	285	306	314	337	344	334
	05-043	152	166	188	209	223	235	249	266	276	286	304	321	332	334
	05-057	169	185	213	224	248	265	290	307	319	335	356	368	372	350
	Mean	**164.2**	**178.6**	**198.8**	**216.8**	**232.3**	**248.3**	**266.5**	**282.1**	**293.1**	**301.6**	**313.5**	**324.8**	**331.4**	**325.4**
	SD	**6.25**	**8.19**	**10.02**	**12.70**	**14.46**	**18.24**	**22.29**	**24.28**	**23.78**	**15.95**	**18.64**	**20.10**	**19.62**	**15.16**

(f) = Animal died on study

Table N-4
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

90-Day Individual Body Weights (grams)
Female Rats

	Animal ID	Day 0	Day 7	Day 14	Day 21	Day 28	Day 35	Day 42	Day 49	Day 56	Day 63	Day 70	Day 77	Day 84	Day 90
Methylcellulose Control	05-076	142	149	156	162	163	173	176	177	181	183	189	188	189	185
	05-077	141	149	151	156	160	161	164	168	170	173	179	166	179	175
	05-084	130	138	145	151	150	153	156	159	161	162	164	172	170	166
	05-088	141	145	150	156	157	160	163	166	168	172	163	163	171	172
	05-098	137	145	152	155	160	161	164	170	174	174	175	176	181	175
	05-100	140	145	153	160	162	166	155	169	175	177	179	183	179	172
	05-101	135	144	149	161	161	168	169	171	180	181	186	186	186	180
	05-114	137	144	153	156	155	156	159	157	163	163	166	169	172	164
	05-120	141	147	152	161	164	168	170	176	178	177	185	187	186	182
	05-127	143	151	158	166	170	171	175	180	181	184	186	186	183	185
	Mean	**138.7**	**145.7**	**151.9**	**158.4**	**160.2**	**163.7**	**165.1**	**169.3**	**173.1**	**174.6**	**177.2**	**177.6**	**179.6**	**175.6**
	SD	**3.97**	**3.62**	**3.60**	**4.35**	**5.41**	**6.53**	**7.34**	**7.39**	**7.34**	**7.56**	**9.82**	**9.56**	**6.74**	**7.38**
4 mg/kg	05-072	140	149	150	151	149	152	158	158	164	164	168	181	174	169
	05-078	136	141	147	156	156	161	164	166	170	171	173	176	175	174
	05-081	130	139	143	151	151	152	156	160	164	169	171	179	175	172
	05-090	140	147	155	162	163	169	171	173	173	179	170	185	183	171
	05-094	144	150	155	159	159	161	166	171	173	174	179	181	179	176
	05-095	136	141	147	154	156	159	148	162	171	173	174	163	176	172
	05-105	137	142	147	155	159	167	169	172	175	174	181	185	183	178
	05-115	144	150	155	162	163	164	166	172	174	179	182	181	182	174
	05-135	146	153	157	165	169	170	173	177	182	186	183	189	186	193
	05-136	136	140	144	146	147	151	154	159	164	166	171	167	169	168
	Mean	**138.9**	**145.2**	**150.0**	**156.1**	**157.2**	**160.6**	**162.5**	**167.0**	**171.0**	**173.5**	**175.2**	**178.7**	**178.2**	**174.7**
	SD	**4.86**	**5.12**	**5.12**	**5.93**	**6.88**	**7.11**	**8.14**	**6.85**	**5.79**	**6.59**	**5.53**	**8.11**	**5.27**	**7.10**
8 mg/kg	05-071	139	145	151	155	156	159	162	167	172	174	176	183	179	176
	05-074	136	136	146	152	154	160	164	166	167	169	171	174	171	166
	05-075	137	141	150	154	155	160	162	164	167	169	171	175	178	165
	05-085	127	131	137	148	149	152	161	174	186	201	213	214	211	204
	05-086	131	137	146	153	158	161	166	171	173	180	186	201	208	195
	05-092	140	144	154	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-102	138	145	151	155	157	166	166	170	173	175	182	181	184	180
	05-106	133	138	147	153	156	159	164	165	169	174	177	179	180	178
	05-108	145	151	156	162	163	170	186	206	209	215	220	222	222	221
	05-112	143	148	156	162	165	172	177	189	196	203	208	222	223	230
	Mean	**136.9**	**141.6**	**149.4**	**154.9**	**157.0**	**162.1**	**167.6**	**174.7**	**179.1**	**184.4**	**189.3**	**194.6**	**195.1**	**190.6**
	SD	**5.45**	**6.11**	**5.74**	**4.54**	**4.74**	**6.19**	**8.40**	**13.98**	**14.78**	**17.16**	**19.09**	**20.28**	**20.63**	**23.51**
10 mg/kg	05-073	134	140	149	153	155	154	162	166	173	178	190	202	210	216
	05-083	141	142	150	156	159	164	169	168	171	174	171	176	174	173
	05-091	134	136	143	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-109	141	145	154	162	160	165	173	179	177	182	184	188	191	183
	05-110	145	147	153	159	161	167	173	176	184	189	196	208	202	205
	05-111	137	143	151	158	157	159	168	177	198	202	210	(f)	(f)	(f)
	05-117	143	150	154	162	163	169	175	174	181	189	195	200	202	207
	05-130	144	146	155	168	173	169	177	190	193	189	202	208	212	206
	05-131	132	138	143	145	149	153	157	158	163	174	178	186	186	191
	05-132	133	137	148	156	160	175	192	203	215	221	222	224	235	226
	Mean	**138.4**	**142.4**	**150.0**	**157.7**	**159.7**	**163.9**	**171.8**	**176.8**	**183.9**	**188.7**	**194.2**	**199.0**	**201.5**	**200.9**
	SD	**4.95**	**4.65**	**4.35**	**6.46**	**6.46**	**7.30**	**9.91**	**13.33**	**15.92**	**15.05**	**15.85**	**15.19**	**18.56**	**17.46**
12 mg/kg	05-080	141	138	153	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-082	126	125	138	145	151	155	161	169	176	191	206	215	217	214
	05-087	134	137	143	149	155	165	174	183	187	189	206	204	204	208
	05-096	133	135	147	150	152	159	151	173	(f)	(f)	(f)	(f)	(f)	(f)
	05-121	135	137	145	149	158	166	171	198	209	227	229	234	232	224
	05-122	129	134	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-123	141	148	157	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-124	130	132	143	151	157	166	176	186	192	189	191	197	199	200
	05-128	137	139	149	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-134	133	139	151	153	158	162	164	170	178	183	193	194	201	193
	Mean	**133.9**	**136.4**	**147.3**	**149.5**	**155.2**	**162.2**	**166.2**	**179.8**	**188.4**	**195.8**	**205.0**	**208.8**	**210.6**	**207.8**
	SD	**4.89**	**5.85**	**5.83**	**2.66**	**3.06**	**4.45**	**9.41**	**11.30**	**13.24**	**17.70**	**15.15**	**16.24**	**13.87**	**12.05**
15 mg/kg	05-093	133	136	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-097	132	137	141	145	151	156	174	190	187	199	202	204	206	203
	05-099	126	132	143	148	163	170	179	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-104	136	136	148	156	171	184	200	207	204	205	215	214	222	213
	05-107	130	129	140	142	167	184	205	216	227	225	228	234	233	230
	05-113	142	148	160	177	201	214	220	231	239	244	251	259	262	258
	05-116	139	137	144	158	170	184	200	212	204	215	226	228	221	217
	05-126	140	140	153	161	171	176	183	190	196	198	(f)	(f)	(f)	(f)
	05-129	136	143	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-133	134	134	147	155	162	165	169	182	189	191	190	204	208	204
	Mean	**134.8**	**137.2**	**147.0**	**155.3**	**169.5**	**179.1**	**191.3**	**204.0**	**206.6**	**211.0**	**218.7**	**223.8**	**225.3**	**220.8**
	SD	**4.85**	**5.43**	**6.72**	**11.00**	**14.36**	**17.38**	**17.65**	**17.43**	**19.52**	**18.48**	**21.44**	**21.17**	**20.53**	**20.70**

(f) = Animal died on study

APPENDIX O

SUMMARY OF 90-DAY FOOD CONSUMPTION AND INDIVIDUAL FOOD CONSUMPTION DATA

Appendix O
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Summary of 90-Day Food Consumption

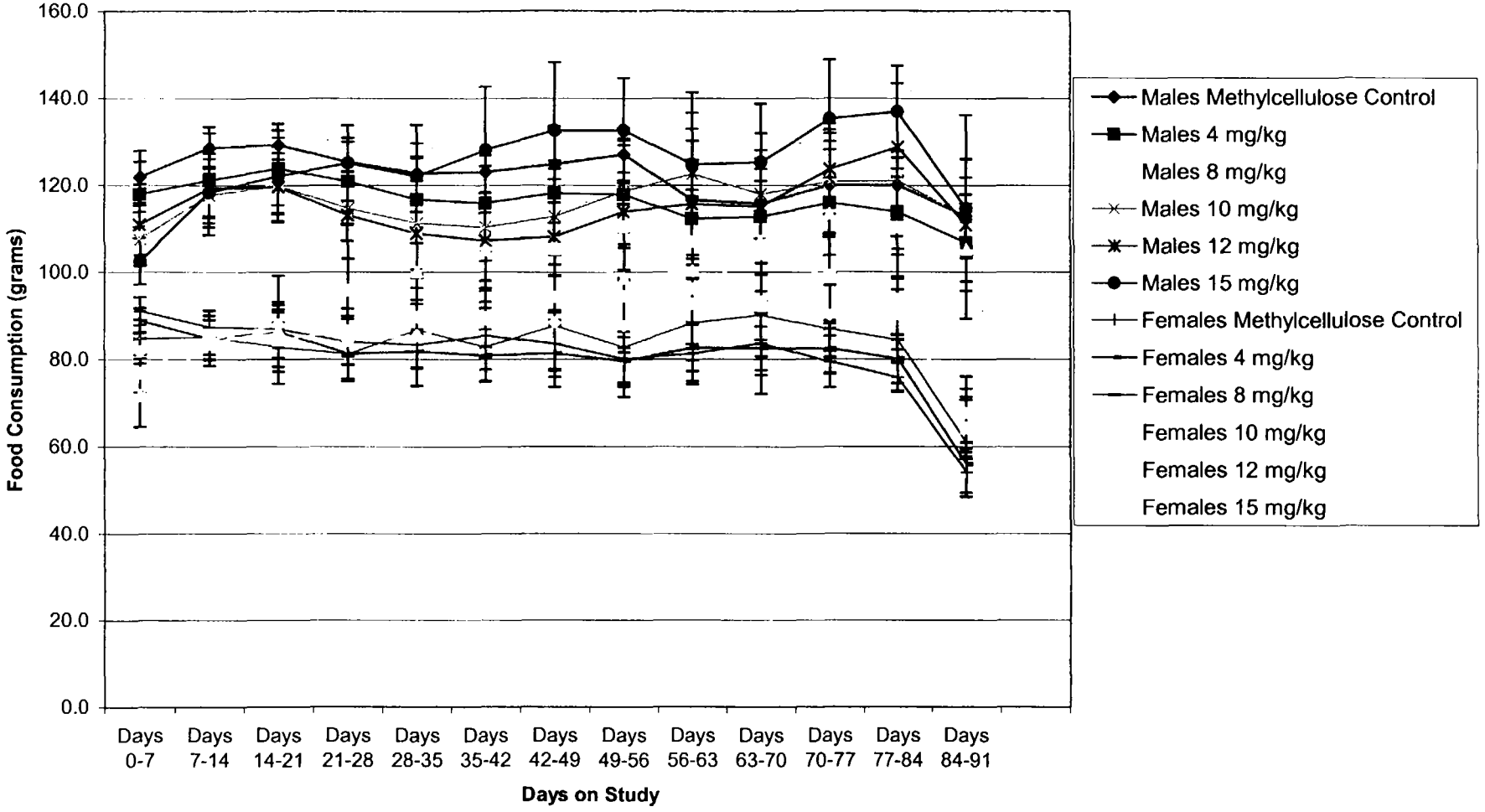


Table O-1
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Summary of Food Consumption (grams)
Male Rats

Period		Methylcellulose Control	RDX in 1% Methylcellulose / 0.2% Tween 80				
			4 mg/kg	8 mg/kg	10 mg/kg	12 mg/kg	15 mg/kg
Days 0-7	Mean	122.0	118.0	109.7*	107.7*	111.0*	102.6*
	S.D.	5.98	7.47	5.70	6.17	9.31	5.32
	N	10	10	10	10	10	10
Days 7-14	Mean	128.6	121.2	117.3*	117.8*	119.3	118.4*
	S.D.	4.79	10.81	8.76	4.87	8.01	5.95
	N	10	10	10	10	10	10
Days 14-21	Mean	129.3	123.9	120.2	119.9	119.6	122.1
	S.D.	3.40	10.25	8.69	4.48	7.79	8.84
	N	10	10	10	10	10	10
Days 21-28	Mean	125.3	120.9	113.1*	114.7*	113.1*	125.1
	S.D.	4.69	9.99	10.09	7.51	9.99	8.69
	N	9	10	10	10	9	10
Days 28-35	Mean	122.8	116.7	109.9*	111.3	108.9*	122.1
	S.D.	6.88	9.98	11.17	14.91	8.31	11.80
	N	10	10	10	9	9	10
Days 35-42	Mean	123.1	115.9	107.0*	110.4	107.3*	128.2
	S.D.	4.93	11.07	11.27	7.78	17.16	14.47
	N	10	10	10	9	9	10
Days 42-49	Mean	124.8	118.1	108.0*	112.8	108.1*	132.6
	S.D.	8.80	14.08	13.30	11.02	17.49	15.61
	N	10	10	10	9	9	10
Days 49-56	Mean	127.1	117.9	110.5*	118.6	113.9	132.6
	S.D.	6.01	12.38	12.41	12.17	15.29	12.06
	N	10	10	10	9	9	9
Days 56-63	Mean	116.6	112.3	107.1	122.6	115.7	124.8
	S.D.	13.63	13.57	11.82	18.74	17.26	11.89
	N	10	10	10	9	9	9
Days 63-70	Mean	115.8	112.8	107.2	118.0	115.1	125.4
	S.D.	8.02	13.38	13.84	14.02	13.01	13.33
	N	10	10	10	9	8	8
Days 70-77	Mean	120.0	116.0	113.5	120.9	123.8	135.3
	S.D.	11.95	12.17	16.58	11.90	10.44	13.54
	N	10	10	10	8	8	8
Days 77-84	Mean	120.0	113.9	110.4	121.1	128.8	136.9*
	S.D.	7.93	9.95	11.52	15.79	14.60	10.56
	N	10	10	9	8	8	8
Days 84-91	Mean	112.9	106.8	105.3	112.7	110.9	114.6
	S.D.	8.89	8.98	9.62	23.45	7.00	11.44
	N	10	10	9	7	8	7

* p less than or equal to 0.05
ANOVA with Holm-Sidak Method

Table O-2
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Summary of Food Consumption (grams)
Female Rats

Period		Methylcellulose Control	RDX in 1% Methylcellulose / 0.2% Tween 80				
			4 mg/kg	8 mg/kg	10 mg/kg	12 mg/kg	15 mg/kg
Days 0-7	Mean	91.1	88.9	84.7*	81.8*	76.8*	71.8*
	S.D.	3.21	2.88	4.47	4.44	4.29	7.28
	N	10	10	10	10	10	10
Days 7-14	Mean	87.4	84.8	85.1	84.5	85.6	83.6
	S.D.	2.63	6.29	3.98	4.48	5.55	3.78
	N	10	10	10	10	9	8
Days 14-21	Mean	87	86.4	82.8	88.0	84.5	86.8
	S.D.	4.42	6.02	5.65	5.07	6.22	12.38
	N	10	10	9	9	6	8
Days 21-28	Mean	84	81.3	81.2	84.3	86.5	95.9*
	S.D.	5.19	6.34	5.7	5.59	5.09	15.23
	N	10	10	9	9	6	8
Days 28-35	Mean	83.3	81.8	86.7	85.4	89.7	100.1*
	S.D.	5.42	7.83	12.84	7.28	3.93	13.79
	N	10	10	9	9	6	8
Days 35-42	Mean	85.4	80.9	82.8	89.2	89.5	105.1*
	S.D.	7.71	5.99	7.71	8.83	6.83	13.29
	N	10	10	9	9	6	8
Days 42-49	Mean	83.5	81.3	87.6	88.4	94.3	105.4*
	S.D.	7.62	7.66	11.74	10.71	17.01	11.63
	N	10	10	9	9	6	7
Days 49-56	Mean	80	79.6	82.7	87.6	94.4	98.6*
	S.D.	6.31	5.44	11.36	12.93	14.77	17.05
	N	10	10	9	9	5	7
Days 56-63	Mean	81.3	82.6	88.3	92.7	96.2	100.4*
	S.D.	6.98	5.34	13.33	10.32	16.5	17.04
	N	10	10	9	9	5	7
Days 63-70	Mean	83.6	82.5	90.1	93.3	104.2*	92.3
	S.D.	7.21	4.99	9.51	8.85	8.61	20.23
	N	10	10	9	9	5	6
Days 70-77	Mean	79.4	82.4	86.9	90.1	98.8*	99.2*
	S.D.	5.87	5.78	10.04	9.6	9.96	17.38
	N	10	10	9	8	5	6
Days 77-84	Mean	75.8	80.1	84.4	90.3*	92.2*	93.8*
	S.D.	3.36	5.63	11.57	8.15	6.72	14.44
	N	10	10	9	8	5	6
Days 84-91	Mean	54.1	56.0	60.9	67.8*	64.2	64.3
	S.D.	4.65	7.53	12.36	8.26	6.46	7.09
	N	10	10	9	8	5	6

* p less than or equal to 0.05
ANOVA with Holm-Sidak Method

Table O-3
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

90-Day Individual Food Consumption (grams)
Male Rats

Group	Animal ID	Day 0-7	Days 7-14	Days 14-21	Days 21-28	Days 28-35	Days 35-42	Days 42-49	Days 49-56	Days 56-63	Days 63-70	Days 70-77	Days 77-84	Days 84-91	Net Change
	05-011	121	130	126	132	134	122	125	124	115	114	129	125	114	1611
Methylcellulose	05-012	125	128	130	128	128	124	123	124	121	116	125	123	115	1610
Control	05-016	121	125	127	120	122	123	121	120	115	105	106	113	103	1521
	05-020	126	129	131	122	118	121	119	126	86	113	102	120	107	1520
	05-023	122	129	132	126	124	129	128	134	118	122	123	118	117	1622
	05-052	114	119	123	118	109	112	107	119	106	103	103	101	95	1429
	05-060	123	131	134	130	117	127	135	133	134	126	136	125	122	1673
	05-064	111	127	129	128	124	121	123	125	114	112	123	128	113	1578
	05-066	125	130	128		127	123	128	129	127	126	124	122	123	1512
	05-070	132	138	133	124	125	129	139	137	130	121	129	125	120	1682
	Mean	**122.0**	**128.6**	**129.3**	**125.3**	**122.8**	**123.1**	**124.8**	**127.1**	**116.6**	**115.8**	**120.0**	**120.0**	**112.9**	**1575.8**
	SD	**5.98**	**4.79**	**3.40**	**4.69**	**6.88**	**4.93**	**8.80**	**6.01**	**13.63**	**8.02**	**11.95**	**7.93**	**8.89**	**79.59**
	05-001	115	114	122	114	116	120	119	115	123	118	117	116	107	1516
4 mg/kg	05-007	125	122	133	132	124	118	133	136	130	123	133	123	108	1640
	05-013	110	108	108	115	104	98	92	94	93	93	96	98	91	1300
	05-028	130	132	127	125	117	120	120	118	114	121	119	117	100	1560
	05-033	115	110	115	115	104	104	106	106	95	99	108	105	96	1378
	05-039	121	128	131	127	128	124	131	126	122	123	124	121	111	1617
	05-041	115	119	119	121	116	118	124	120	109	114	120	119	114	1528
	05-055	126	134	138	135	130	131	133	131	127	132	130	125	115	1687
	05-062	117	136	134	124	124	125	122	123	113	111	114	117	120	1580
	05-067	106	109	112	101	104	101	101	110	97	94	99	98	106	1338
	Mean	**118.0**	**121.2**	**123.9**	**120.9**	**116.7**	**115.9**	**118.1**	**117.9**	**112.3**	**112.8**	**116.0**	**113.9**	**106.8**	**1514.4**
	SD	**7.47**	**10.81**	**10.25**	**9.99**	**9.98**	**11.07**	**14.08**	**12.38**	**13.57**	**13.38**	**12.17**	**9.95**	**8.98**	**132.65**
	05-003	103	103	104	93	90	87	82	90	86	87	90	97	94	1206
8 mg/kg	05-006	106	109	117	110	97	101	102	101	95	99	98	101	101	1337
	05-015	113	113	116	117	102	101	94	91	92	89	92	95	87	1302
	05-034	98	111	108	98	102	92	100	120	113	123	131	130	114	1440
	05-037	111	118	123	114	115	110	112	111	112	107	111	118	105	1467
	05-045	112	123	127	119	120	115	109	116	119	129	137	(f)	(f)	1326
	05-046	113	115	124	119	114	114	120	126	119	117	125	121	115	1542
	05-051	110	122	126	121	118	122	121	119	116	111	124	110	110	1530
	05-068	116	130	129	116	121	115	119	118	111	111	121	110	110	1527
	05-069	115	129	128	124	120	113	121	113	108	99	106	112	112	1500
	Mean	**109.7**	**117.3**	**120.2**	**113.1**	**109.9**	**107.0**	**108.0**	**110.5**	**107.1**	**107.2**	**113.5**	**110.4**	**105.3**	**1417.7**
	SD	**5.70**	**8.76**	**8.69**	**10.09**	**11.17**	**11.27**	**13.30**	**12.41**	**11.82**	**13.84**	**16.58**	**11.52**	**9.62**	**116.83**
	05-017	100	110	119	104	103	111	130	134	133	122	(f)	(f)	(f)	1166
10 mg/kg	05-024	97	121	115	111	112	113	117	120	111	105	113	99	66	1400
	05-040	114	114	117	104	108	105	106	110	110	125	123	128	132	1496
	05-042	109	119	121	117	142	108	123	132	163	130	138	140	123	1665
	05-049	107	113	120	123	118	108	102	107	110	107	115	118	114	1462
	05-050	109	123	123	122	85	119	109	110	108	108	110	102	99	1427
	05-053	110	113	112	112	108	99	97	103	110	99	105	112	125	1405
	05-054	117	120	126	125	112	125	123	134	138	142	131	133		1526
	05-056	103	124	126	111		(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	464
	05-065	111	121	120	118	114	106	108	117	120	124	132	137	130	1558
	Mean	**107.7**	**117.8**	**119.9**	**114.7**	**111.3**	**110.4**	**112.8**	**118.6**	**122.6**	**118.0**	**120.9**	**121.1**	**112.7**	**1356.9**
	SD	**6.17**	**4.87**	**4.48**	**7.51**	**14.91**	**7.78**	**11.02**	**12.17**	**18.74**	**14.02**	**11.90**	**15.79**	**23.45**	**339.47**
	05-005	95	108	107	108	102	106	104	106	122	122	134	138	106	1458
12 mg/kg	05-009	105	105	112	107	96	88	92	106	99	97	104	108	97	1316
	05-019	121	126	122	119	119	133	121	133	147	(f)	(f)	(f)	(f)	1141
	05-021	117	122	124	118	109	107	111	115	107	120	126	146	111	1533
	05-027	124	124	123	121	116	109	114	110	114	117	124	125	113	1534
	05-031	109	116	111	96	104	80	88	99	102	105	115	114	109	1348
	05-047	104	119	115	105	103	99	84	92	95	100	121	117	116	1370
	05-048	104	124	124	115	111	116	124	130	120	128	135	143	116	1590
	05-058	111	118	130	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	359
	05-063	120	131	128	129	120	128	135	134	135	132	131	139	119	1681
	Mean	**111.0**	**119.3**	**119.6**	**113.1**	**108.9**	**107.3**	**108.1**	**113.9**	**115.7**	**115.1**	**123.8**	**128.8**	**110.9**	**1333.0**
	SD	**9.31**	**8.01**	**7.79**	**9.99**	**8.31**	**17.16**	**17.49**	**15.29**	**17.26**	**13.01**	**10.44**	**14.60**	**7.00**	**375.74**
	05-008	97	124	138	138	136	154	167	157	106	(f)	(f)	(f)	(f)	1217
15 mg/kg	05-010	108	113	113	117	117	117	137	134	130	134	141	137		1498
	05-018	99	108	106	121	107	121	112	126	137	123	127	129	118	1534
	05-022	105	116	121	122	129	136	131	131	115	123	120	126	103	1578
	05-025	109	119	125	132	138	141	144	(f)	(f)	(f)	(f)	(f)	(f)	908
	05-030	92	121	122	134	120	126	127	139	123	110	133	134	104	1585
	05-032	102	114	119	124	103	113	124	121	123	108	116	124	107	1498
	05-035	103	120	121	110	116	111	119	117	132	129	142	144	127	1591
	05-043	104	120	131	121	123	120	124	127	114	126	152	149	132	1643
	05-057	107	129	125	132	132	143	141	141	143	150	151	152	111	1757
	Mean	**102.6**	**118.4**	**122.1**	**125.1**	**122.1**	**128.2**	**132.6**	**132.6**	**124.8**	**125.4**	**135.3**	**136.9**	**114.6**	**1480.9**
	SD	**5.32**	**5.95**	**8.84**	**8.69**	**11.80**	**14.47**	**15.61**	**12.06**	**11.89**	**13.33**	**13.54**	**10.56**	**11.44**	**244.08**

= No data
(f) = Animal died on study

Table O-4
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

90-Day Individual Food Consumption (grams)
Female Rats

	Animal ID	Days 0-7	Days 7-14	Days 14-21	Days 21-28	Days 28-35	Days 35-42	Days 42-49	Days 49-56	Days 56-63	Days 63-70	Days 70-77	Days 77-84	Days 84-90	Net Change
Methylcellulose Control	05-076	94	90	86	85	91	94	88	84	89	93	81	79	57	1111
	05-077	91	85	86	81	80	81	80	78	83	86	79	78	56	1044
	05-084	89	83	83	78	78	79	76	72	75	77	80	72	54	996
	05-088	91	86	84	83	77	86	79	76	79	76	72	74	52	1015
	05-098	96	89	85	85	83	84	87	82	79	82	82	77	50	1061
	05-100	92	91	95	87	84	91	92	90	87	91	87	73	49	1109
	05-101	84	85	86	82	87	82	85	82	85	85	81	81	53	1058
	05-114	90	90	83	76	76	71	68	69	66	71	67	72	48	947
	05-120	93	87	87	90	90	89	91	85	82	91	85	79	60	1109
	05-127	91	88	95	93	87	97	89	82	88	84	80	73	62	1109
	Mean	91.1	87.4	87.0	84.0	83.3	85.4	83.5	80.0	81.3	83.6	79.4	75.8	54.1	1055.9
	SD	3.21	2.63	4.42	5.19	5.42	7.71	7.62	6.31	6.98	7.21	5.87	3.36	4.65	56.56
4 mg/kg	05-072	87	79	78	71	74	73	66	77	71	74	80	72	51	953
	05-078	88	87	88	79	84	83	78	77	78	81	80	76	57	1036
	05-081	85	77	81	75	67	76	73	71	83	76	83	90	51	988
	05-090	87	93	94	84	91	92	89	83	84	85	90	83	47	1102
	05-094	91	87	85	78	78	79	82	75	82	81	77	75	56	1026
	05-095	87	87	89	88	87	81	85	84	86	85	78	79	54	1070
	05-105	87	81	86	86	88	81	85	83	83	83	89	85	59	1076
	05-115	91	85	90	86	83	86	84	87	88	91	85	84	56	1096
	05-135	94	95	95	90	90	85	92	85	90	87	89	82	75	1149
	05-136	92	77	78	76	76	73	79	74	81	82	73	75	54	990
	Mean	88.9	84.8	86.4	81.3	81.8	80.9	81.3	79.6	82.6	82.5	82.4	80.1	56.0	1048.6
	SD	2.88	6.29	6.02	6.34	7.83	5.99	7.66	5.44	5.34	4.99	5.78	5.63	7.53	60.83
8 mg/kg	05-071	89	87	84	80	80	75	84	85	84	88	90	83	57	1066
	05-074	75	81	80	76	78	79	77	71	72	78	71	71	48	957
	05-075	84	81	77	78	74	75	74	68	72	78	74	72	43	950
	05-085	81	80	84	77	118	82	89	90	107	101	92	72	57	1130
	05-086	82	85	83	85	83	88	85	76	83	88	90	102	64	1094
	05-092	86	89	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	175
	05-102	87	81	72	76	84	73	84	78	82	84	80	85	59	1025
	05-106	90	89	89	89	87	90	83	85	91	91	88	83	64	1119
	05-108	88	88	87	79	84	94	112	106	108	100	95	96	71	1208
	05-112	85	90	89	91	92	89	100	85	96	103	102	96	85	1203
	Mean	84.7	85.1	82.8	81.2	86.7	82.8	87.6	82.7	88.3	90.1	86.9	84.4	60.9	992.7
	SD	4.47	3.98	5.65	5.70	12.84	7.71	11.74	11.36	13.33	9.51	10.04	11.57	12.36	300.70
10 mg/kg	05-073	80	83	83	79	77	77	80	73	88	88	95	98	80	1081
	05-083	80	87	88	82	85	87	81	79	79	80	77	76	55	1036
	05-091	75	78	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	153
	05-109	80	87	93	85	89	92	92	87	89	88	87	92	61	1122
	05-110	80	84	88	84	91	90	86	86	86	103	98	89	77	1142
	05-111	80	81	87	75	78	86	85	102	103	96	(f)	(f)	(f)	873
	05-117	86	82	91	86	85	85	88	88	96	90	89	94	67	1127
	05-130	90	81	97	94	79	93	88	82	97	92	79	86	63	1121
	05-131	87	89	81	84	85	84	81	77	84	93	90	85	71	1091
	05-132	80	93	84	90	100	109	115	114	112	110	106	102	68	1283
	Mean	81.8	84.5	88.0	84.3	85.4	89.2	88.4	87.6	92.7	93.3	90.1	90.3	67.8	1002.9
	SD	4.44	4.48	5.07	5.59	7.28	8.83	10.71	12.93	10.32	8.85	9.60	8.15	8.26	315.44
12 mg/kg	05-080	71	87	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	158
	05-082	73	80	85	84	85	85	81	87	94	114	107	100	74	1149
	05-087	79	80	83	85	92	98	93	87	90	105	97	91	63	1143
	05-096	79	82	80	81	87	85	89	(f)	(f)	(f)	(f)	(f)	(f)	583
	05-121	72	84	76	84	90	81	125	120	125	110	111	96	63	1237
	05-122	77	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	77
	05-123	82	95	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	177
	05-124	73	85	92	90	96	96	100	94	88	92	88	82	65	1141
	05-128	79	83	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	162
	05-134	83	94	91	95	88	92	78	84	84	100	91	92	56	1128
	Mean	76.8	85.6	84.5	86.5	89.7	89.5	94.3	94.4	96.2	104.2	98.8	92.2	64.2	695.5
	SD	4.29	5.55	6.22	5.09	3.93	6.83	17.01	14.77	16.50	8.61	9.96	6.72	6.46	507.96
15 mg/kg	05-093	72	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	72
	05-097	75	81	77	75	85	92	104	81	92	91	76	80	64	1073
	05-099	74	85	78	94	104	102	(f)	(f)	(f)	(f)	(f)	(f)	(f)	537
	05-104	71	82	82	96	102	110	98	94	90	100	84	95	60	1164
	05-107	65	83	76	108	115	117	120	127	117	100	107	100	73	1308
	05-113	86	91	114	125	122	128	112	118	126	118	124	119	73	1456
	05-116	67	78	88	89	100	106	118	92	107	57	107	83	57	1149
	05-126	65	84	88	96	89	99	97	90	77	(f)	(f)	(f)	(f)	785
	05-129	80	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	80
	05-133	63	85	91	84	84	87	89	88	94	88	97	86	59	1095
	Mean	71.8	83.6	86.8	95.9	100.1	105.1	105.4	98.6	100.4	92.3	99.2	93.8	64.3	871.9
	SD	7.28	3.78	12.38	15.23	13.79	13.29	11.63	17.05	17.04	20.23	17.38	14.44	7.09	491.07

(f) = Animal died on study

APPENDIX P

SUMMARY OF 90-DAY FOOD EFFICIENCY AND INDIVIDUAL FOOD EFFICIENCY DATA

Appendix P
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Summary of 90-Day Food Efficiency

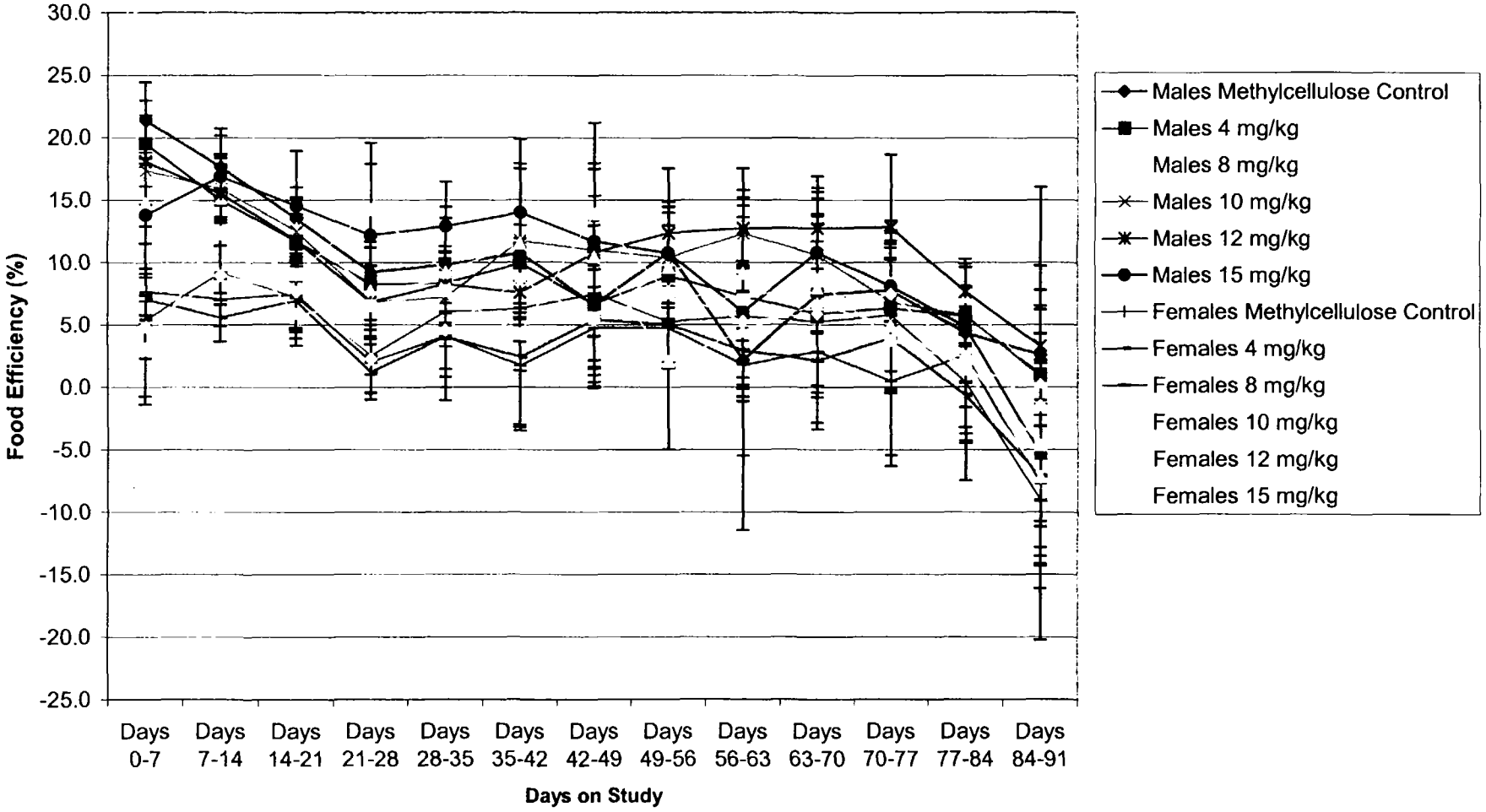


Table P-1
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Summary of Food Efficiency (%)
Male Rats

Period		Methylcellulose Control	RDX in 1% Methylcellulose / 0.2% Tween 80				
			4 mg/kg	8 mg/kg	10 mg/kg	12 mg/kg	15 mg/kg
Day 0-7	Mean	21.44	19.60	14.79*	17.42	18.15	13.86*
	S.D.	3.070	3.440	3.200	4.450	3.480	5.000
	N	10	10	10	10	10	10
Day 7-14	Mean	17.70	15.05	15.27	15.94	15.58	16.95
	S.D.	3.070	3.680	3.360	2.470	2.330	3.260
	N	10	10	10	10	10	10
Day 14-21	Mean	13.50	11.73	12.79	12.50	11.78	14.56
	S.D.	1.740	4.310	2.350	1.390	1.810	4.370
	N	10	10	10	10	10	10
Day 21-28	Mean	9.26	8.30	7.81	6.84	6.85	12.2
	S.D.	2.790	2.910	3.870	2.910	4.850	5.690
	N	9	10	10	10	10	10
Day 28-35	Mean	9.83	8.36	8.61	7.21	8.31	12.92
	S.D.	1.070	2.420	2.680	7.230	4.460	3.530
	N	10	10	10	9	9	10
Day 35-42	Mean	10.77	9.95	7.75	11.77	7.58	14.02
	S.D.	2.230	3.990	2.800	8.120	3.890	3.910
	N	10	10	10	9	9	10
Day 42-49	Mean	6.60	6.69	5.63	11.01	10.81	11.7
	S.D.	4.440	6.290	4.140	6.950	6.710	3.660
	N	10	10	10	9	9	10
Day 49-56	Mean	10.80	8.94	9.64	10.42	12.38	10.79
	S.D.	4.060	1.790	4.850	4.030	5.170	2.190
	N	10	10	10	9	9	9
Day 56-63	Mean	2.18	7.32	9.17	12.33*	12.76*	6.03
	S.D.	13.630	1.760	4.460	2.220	3.080	11.530
	N	10	10	10	9	9	9
Day 63-70	Mean	7.43	5.90	7.95	10.64	12.76*	10.83
	S.D.	8.250	1.420	5.150	6.300	3.250	2.900
	N	10	10	10	9	9	8
Day 70-77	Mean	7.78	6.35	8.36	6.84	12.86	8.13
	S.D.	2.470	1.420	3.150	5.560	5.790	4.420
	N	10	10	10	8	8	8
Day 77-84	Mean	4.35	5.74	7.24	5.78	7.68*	4.85
	S.D.	2.090	2.270	3.050	4.130	1.950	1.600
	N	10	10	9	8	8	8
Day 84-91	Mean	2.59	1.02	0.39	0.88	3.31	-5.32
	S.D	3.630	3.290	6.130	15.180	6.410	7.510
	N	10	10	9	7	8	7
Total	Mean	123.25	114.96	114.64	120.44	127.61	126.65
	S.D.	11.240	11.450	17.730	29.840	28.510	14.150
	N	10	10	10	10	8	10

* p less than or equal to 0.05
ANOVA with Holm-Sidak Method

Table P-2
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Summary of Food Efficiency (%)
Female Rats

Period		Methylcellulose Control	RDX in 1% Methylcellulose / 0.2% Tween 80				
			4 mg/kg	8 mg/kg	10 mg/kg	12 mg/kg	15 mg/kg
Day 0-7	Mean	7.71	7.11	5.47	4.87	3.10*	3.01*
	S.D.	1.862	2.040	2.237	2.566	3.846	4.387
	N	10	10	10	10	10	10
Day 7-14	Mean	7.06	5.61	9.18	8.98	12.49*	12.34*
	S.D.	2.168	1.939	2.219	2.365	3.252	3.622
	N	10	10	10	9	9	8
Day 14-21	Mean	7.44	6.95	7.21	7.70	5.90	9.09
	S.D.	3.069	3.076	2.489	3.066	2.599	4.551
	N	10	10	9	9	6	8
Day 21-28	Mean	2.05	1.22	2.55	2.29	6.55	14.27*
	S.D.	2.537	2.212	1.535	2.688	2.693	5.316
	N	10	10	9	9	6	8
Day 28-35	Mean	4.09	4.08	6.05	4.56	7.74	9.25*
	S.D.	3.277	2.642	2.804	5.626	2.580	4.318
	N	10	10	9	9	6	8
Day 35-42	Mean	1.75	2.45	6.29	8.66*	4.27	11.54*
	S.D.	4.946	5.950	4.974	3.252	7.279	5.972
	N	10	10	9	9	6	8
Day 42-49	Mean	4.76	5.42	7.51	5.42	13.93*	10.50
	S.D.	4.689	4.456	5.887	5.492	7.268	3.295
	N	10	10	9	9	6	7
Day 49-56	Mean	4.75	5.06	5.25	7.73	7.54	2.07
	S.D.	3.151	3.062	3.624	6.258	2.051	7.051
	N	10	10	9	9	5	7
Day 56-63	Mean	1.79	2.94	5.69	5.27	7.02	4.49
	S.D.	1.920	2.771	3.841	4.521	8.174	5.260
	N	10	10	9	9	5	7
Day 63-70	Mean	2.89	2.16	5.29	5.92	8.67	6.73
	S.D.	5.731	5.558	3.226	5.795	6.473	7.168
	N	10	10	9	9	5	6
Day 70-77	Mean	0.50	3.94	5.78	7.49	3.75	4.97
	S.D.	6.816	9.407	5.973	3.689	4.258	5.389
	N	10	10	9	8	5	6
Day 77-84	Mean	2.58	-0.63	0.40	2.45	1.99	1.44
	S.D.	7.036	6.858	4.130	5.657	3.617	5.741
	N	10	10	9	8	5	6
Day 84-91	Mean	-7.74	-7.10	-9.06	-1.47	-4.63	-7.18
	S.D.	6.405	9.015	11.178	9.262	8.906	3.997
	N	10	10	9	8	5	6
Total	Mean	39.64	39.20	57.46	67.77	79.32	83.53
	S.D.	7.241	9.847	23.348	20.137	12.095	9.531
	N	10	10	9	8	5	6

* p less than or equal to 0.05
ANOVA with Holm-Sidak Method

Table P-3
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

90-Day Individual Food Efficiency (%)
Male Rats

Group	Animal ID	Day 0-7	Days 7-14	Days 14-21	Days 21-28	Days 28-35	Days 35-42	Days 42-49	Days 49-56	Days 56-63	Days 63-70	Days 70-77	Days 77-84	Days 84-91	Total
	05-011	21.49	23.08	12.70	12.12	9.70	9.02	7.20	12.10	4.35	7.90	9.30	0.80	8.77	138.52
Methylcellulose	05-012	22.40	17.97	10.77	11.72	10.16	11.29	6.50	9.68	7.44	5.17	9.60	1.63	0.87	125.19
Control	05-016	24.79	17.60	14.96	10.00	10.66	12.20	8.26	7.50	4.35	2.86	5.66	6.20	1.94	126.97
	05-020	23.81	19.38	15.27	4.10	11.02	5.79	-4.20	20.64	-36.05	30.09	6.86	6.67	7.48	110.84
	05-023	20.49	18.61	15.91	7.14	9.68	12.40	8.59	11.19	5.93	4.10	6.50	3.39	1.71	125.65
	05-052	21.05	18.49	12.20	9.32	7.34	10.71	5.61	11.77	2.83	3.88	7.77	3.96	2.11	117.03
	05-060	20.33	17.56	13.43	10.77	10.26	11.81	12.59	7.52	8.96	9.52	8.09	6.40	3.28	140.51
	05-064	25.23	18.90	14.73	11.72	10.48	9.92	8.94	6.40	5.26	2.68	13.01	3.91	-3.54	127.63
	05-066	14.40	13.08	13.28		10.24	10.57	3.91	12.40	10.24	3.97	4.03	6.56	4.07	106.73
	05-070	20.46	12.32	11.28	6.45	8.80	13.95	8.63	8.76	8.46	4.13	6.98	4.00	-0.83	113.39
	Mean	**21.45**	**17.70**	**13.45**	**9.26**	**9.83**	**10.77**	**6.60**	**10.80**	**2.18**	**7.43**	**7.78**	**4.35**	**2.59**	**123.25**
	SD	**3.072**	**3.074**	**1.743**	**2.787**	**1.069**	**2.231**	**4.440**	**4.063**	**13.634**	**8.254**	**2.467**	**2.089**	**3.628**	**11.237**
	05-001	18.26	11.40	13.93	7.02	13.79	14.17	0.84	11.30	7.32	5.93	3.42	3.45	3.74	114.58
4 mg/kg	05-007	22.40	12.30	13.53	10.61	6.45	0.85	23.31	8.09	8.46	4.07	6.77	7.32	0	124.14
	05-013	14.55	12.96	6.48	7.83	6.73	8.16	1.09	10.64	6.45	4.30	6.25	6.12	2.20	93.76
	05-028	20.77	15.91	9.45	3.20	6.84	14.17	7.50	10.17	3.51	7.44	5.88	3.42	-5.00	103.25
	05-033	20.87	11.82	2.61	12.17	8.65	11.54	6.60	9.43	7.37	8.08	8.33	5.71	0	113.20
	05-039	23.97	14.84	15.27	8.66	10.94	8.87	6.87	7.94	8.20	7.32	8.07	2.48	0	123.41
	05-041	19.13	19.33	13.45	12.40	6.03	13.56	4.03	9.17	8.26	6.14	6.67	5.88	4.39	128.43
	05-055	20.64	17.91	16.67	8.15	9.23	10.69	6.77	5.34	10.24	6.06	6.92	5.60	-0.87	123.34
	05-062	22.22	22.06	13.43	8.07	7.26	9.60	4.92	7.32	6.20	5.41	6.14	10.26	-0.83	122.04
	05-067	13.21	11.93	12.50	4.95	7.69	7.92	4.95	10.00	7.22	4.26	5.05	7.14	6.60	103.42
	Mean	**19.60**	**15.05**	**11.73**	**8.31**	**8.36**	**9.95**	**6.69**	**8.94**	**7.32**	**5.90**	**6.35**	**5.74**	**1.02**	**114.96**
	SD	**3.435**	**3.679**	**4.313**	**2.914**	**2.419**	**3.988**	**6.287**	**1.786**	**1.765**	**1.417**	**1.415**	**2.269**	**3.294**	**11.453**
	05-003	12.62	7.77	12.50	3.23	7.78	4.60	4.88	13.33	3.49	12.64	5.56	11.34	2.13	101.86
8 mg/kg	05-006	11.32	16.51	14.53	4.55	4.12	7.92	6.86	7.92	7.37	10.10	5.10	5.94	12.87	115.12
	05-015	10.62	11.50	7.76	0.86	8.82	6.93	0	7.69	6.52	3.37	8.70	10.53	-5.75	77.55
	05-034	20.41	14.41	12.96	12.25	12.75	9.78	0	20.00	10.62	13.01	13.74	7.69	-6.14	141.48
	05-037	16.22	16.95	14.63	8.77	10.44	3.64	6.25	9.91	10.71	7.48	6.31	9.32	-5.71	114.91
	05-045	11.61	17.89	14.96	6.72	11.67	7.83	0.92	9.48	20.17	15.50	13.87	(f)	(f)	130.61
	05-046	17.70	15.65	12.10	11.77	7.90	8.77	11.67	13.49	5.88	9.40	6.40	4.13	4.35	129.20
	05-051	14.55	18.03	15.08	9.92	9.32	13.12	7.44	5.04	8.62	5.41	8.87	1.82	1.82	119.03
	05-068	16.38	15.39	10.08	11.21	8.26	9.57	8.40	4.24	9.01	3.60	6.61	6.36	-1.82	107.29
	05-069	16.52	18.61	13.28	8.87	5.00	5.31	9.92	5.31	9.26	-1.01	8.49	8.04	1.79	109.38
	Mean	**14.80**	**15.27**	**12.79**	**7.82**	**8.61**	**7.75**	**5.63**	**9.64**	**9.17**	**7.95**	**8.37**	**7.24**	**0.39**	**114.64**
	SD	**3.196**	**3.356**	**2.353**	**3.866**	**2.686**	**2.804**	**4.135**	**4.850**	**4.462**	**5.144**	**3.149**	**3.048**	**6.133**	**17.725**
	05-017	20.00	19.09	14.29	2.89	12.62	18.02	20.77	15.67	9.77	-3.28	(f)	(f)	(f)	129.84
10 mg/kg	05-024	13.40	19.84	13.04	8.11	13.39	8.85	5.13	6.67	10.81	7.62	0.89	6.06	-31.82	81.98
	05-040	18.42	14.04	11.11	3.85	4.63	9.52	16.04	15.46	12.73	16.80	4.88	10.16	8.33	145.95
	05-042	11.93	16.81	13.22	5.13	7.04	15.74	17.07	8.33	14.11	9.23	10.87	0.71	0	130.20
	05-049	10.28	13.27	13.33	7.32	9.32	6.48	2.94	5.61	13.64	13.08	7.83	9.32	5.26	117.69
	05-050	19.27	17.89	13.82	10.66	14.12	4.20	3.67	7.27	8.33	7.41	6.36	10.78	3.03	126.81
	05-053	17.27	12.39	10.71	7.14	7.41	5.05	4.12	9.71	14.55	14.14	9.52	6.25	15.20	133.47
	05-054	22.22	15.83	13.49	11.20	-9.82	29.60	15.45	9.70	14.49	16.20	-1.53	1.50		138.34
	05-056	24.27	14.52	11.11	3.60		(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	53.50
	05-065	17.12	15.70	10.83	8.48	6.14	8.49	13.89	15.39	12.50	14.52	15.91	1.46	6.15	146.57
	Mean	**17.42**	**15.94**	**12.50**	**6.84**	**7.21**	**11.77**	**11.01**	**10.42**	**12.33**	**10.64**	**6.84**	**5.78**	**0.88**	**120.44**
	SD	**4.453**	**2.475**	**1.386**	**2.910**	**7.225**	**8.120**	**6.949**	**4.034**	**2.223**	**6.299**	**5.557**	**4.135**	**15.178**	**29.843**
	05-005	21.05	15.74	13.08	7.41	12.75	7.55	22.12	9.43	16.39	14.75	17.16	6.52	-1.89	162.07
12 mg/kg	05-009	20.00	13.33	12.50	5.61	2.08	5.68	9.78	17.93	7.07	14.43	8.65	6.48	8.25	131.80
	05-019	19.84	15.08	8.20	17.65	14.29	12.78	2.48	10.53	15.65	(f)	(f)	(f)	(f)	116.48
	05-021	17.95	15.57	13.71	5.09	8.26	3.74	9.01	13.91	9.35	15.00	11.91	10.27	-5.41	128.35
	05-027	18.55	12.90	13.01	4.96	3.45	8.26	14.91	5.46	12.28	15.39	8.87	8.00	8.85	134.88
	05-031	12.84	12.93	9.91	0	5.77	2.50	11.36	20.20	11.77	7.62	20.00	9.65	7.34	131.89
	05-047	12.50	17.65	10.44	3.81	4.85	5.05	0	14.13	14.74	14.00	19.84	7.69	9.48	134.17
	05-048	15.39	18.55	13.71	7.83	11.71	8.62	12.10	14.62	15.00	13.28	12.59	4.20	-5.17	142.41
	05-058	22.52	19.49	11.54	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	53.55
	05-063	20.83	14.50	11.72	9.30	11.67	14.06	15.56	5.22	12.59	7.58	3.82	8.63	5.04	140.53
	Mean	**18.15**	**15.57**	**11.78**	**6.85**	**8.31**	**7.58**	**10.81**	**12.38**	**12.76**	**12.76**	**12.86**	**7.68**	**3.31**	**127.61**
	SD	**3.479**	**2.336**	**1.806**	**4.851**	**4.461**	**3.891**	**6.706**	**5.168**	**3.076**	**3.246**	**5.788**	**1.945**	**6.407**	**28.508**
	05-008	11.34	21.77	22.46	12.32	16.18	16.23	10.78	9.55	-19.81	(f)	(f)	(f)	(f)	100.83
15 mg/kg	05-010	22.22	15.04	10.62	11.11	16.24	7.69	17.52	12.69	3.85	13.43	3.55	5.84		139.80
	05-018	6.06	12.96	10.38	16.53	7.48	14.05	6.25	11.11	19.71	9.76	5.51	3.88	-4.24	119.43
	05-022	15.24	18.97	10.74	16.39	13.95	11.77	9.16	12.21	0	10.57	4.17	5.56	-7.77	120.96
	05-025	18.35	12.61	16.80	18.18	14.49	17.73	13.19	(f)	(f)	(f)	(f)	(f)	(f)	111.35
	05-030	8.70	17.36	14.75	11.94	17.50	15.08	8.66	11.51	3.25	8.18	11.28	2.99	0.96	132.16
	05-032	9.80	15.79	15.97	4.84	7.77	19.47	8.87	9.09	11.38	10.19	5.17	5.65	0	123.98
	05-035	18.45	15.00	19.01	0.91	12.93	9.01	16.81	14.53	15.91	6.20	16.20	4.86	-7.87	141.94
	05-043	13.46	18.33	16.03	11.57	9.76	11.67	13.71	7.87	8.77	14.29	11.18	7.38	1.52	145.54
	05-057	14.95	21.71	8.80	18.18	12.88	17.48	12.06	8.51	11.19	14.00	7.95	2.63	-19.82	130.52
	Mean	**13.86**	**16.95**	**14.56**	**12.20**	**12.92**	**14.02**	**11.70**	**10.79**	**6.03**	**10.83**	**8.13**	**4.85**	**-5.32**	**126.65**
	SD	**4.996**	**3.259**	**4.374**	**5.687**	**3.532**	**3.904**	**3.661**	**2.191**	**11.533**	**2.900**	**4.419**	**1.597**	**7.511**	**14.147**

= no data
(f) = Animal died on study

Table P-4
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

90-Day Individual Food Efficiency (%)
Female Rats

Group	Animal ID	Day 0-7	Days 7-14	Days 14-21	Days 21-28	Days 28-35	Days 35-42	Days 42-49	Days 49-56	Days 56-63	Days 63-70	Days 70-77	Days 77-84	Days 84-91	Total
	05-076	7.45	7.78	6.98	1.18	10.99	3.19	1.14	4.76	2.25	6.45	-1.23	1.27	-7.02	45.17
Methylcellulose	05-077	8.79	2.35	5.81	4.94	1.25	3.70	5.00	2.56	3.61	6.98	-16.46	16.67	-7.14	38.07
Control	05-084	8.99	8.43	7.23	-1.28	3.85	3.80	3.95	2.78	1.33	2.60	10.00	-2.78	-7.41	41.48
	05-088	4.40	5.81	7.14	1.20	3.90	3.49	3.80	2.63	5.06	-11.84	0	10.81	1.92	38.33
	05-098	8.33	7.87	3.53	5.88	1.20	3.57	6.90	4.88	0	1.22	1.22	6.49	-12.00	39.09
	05-100	5.43	8.79	7.37	2.30	4.76	-12.09	15.22	6.67	2.30	2.20	4.60	-5.48	-14.29	27.78
	05-101	10.71	5.88	13.95	0	8.05	1.22	2.35	10.98	1.18	5.88	0	0.00	-11.32	48.88
	05-114	7.78	10.00	3.61	-1.32	1.32	4.23	-2.94	8.70	0	4.23	4.48	4.17	-16.67	27.58
	05-120	6.45	5.75	10.34	3.33	4.44	2.25	6.59	2.35	-1.22	8.79	2.35	-1.27	-6.67	43.51
	05-127	8.79	7.95	8.42	4.30	1.15	4.12	5.62	1.22	3.41	2.38	0	-4.11	3.23	46.48
	Mean	**7.71**	**7.06**	**7.44**	**2.05**	**4.09**	**1.75**	**4.76**	**4.75**	**1.79**	**2.89**	**0.50**	**2.58**	**-7.74**	**39.64**
	SD	**1.862**	**2.168**	**3.069**	**2.537**	**3.277**	**4.946**	**4.689**	**3.151**	**1.920**	**5.731**	**6.816**	**7.036**	**6.405**	**7.241**
	05-072	10.34	1.27	1.28	-2.82	4.05	8.22	0	7.79	0	5.41	16.25	-9.72	-9.80	32.27
4 mg/kg	05-078	5.68	6.90	10.23	0	5.95	3.61	2.56	5.19	1.28	2.47	3.75	-1.32	-1.75	44.56
	05-081	10.59	5.19	9.88	0	1.49	5.26	5.48	5.63	6.02	2.63	9.64	-4.44	-5.88	51.50
	05-090	8.05	8.60	7.45	1.19	6.59	2.17	2.25	0	7.14	-10.59	16.67	-2.41	-25.53	21.58
	05-094	6.59	5.75	4.71	0	2.56	6.33	6.10	2.67	1.22	6.17	2.60	-2.67	-5.36	36.67
	05-095	5.75	6.90	7.87	2.27	3.45	-13.58	16.47	10.71	2.33	1.18	-14.10	16.46	-7.41	38.28
	05-105	5.75	6.17	9.30	4.65	9.09	2.47	3.53	3.61	-1.20	8.43	4.49	-2.35	-8.47	45.47
	05-115	6.59	5.88	7.78	1.16	1.20	2.33	7.14	2.30	5.68	3.30	-1.18	1.19	-14.29	29.10
	05-135	7.45	4.21	8.42	4.44	1.11	3.53	4.35	5.88	4.44	-3.45	6.74	-3.66	9.33	52.81
	05-136	4.35	5.19	2.56	1.32	5.26	4.11	6.33	6.76	2.47	6.10	-5.48	2.67	-1.85	39.78
	Mean	**7.11**	**5.61**	**6.95**	**1.22**	**4.08**	**2.45**	**5.42**	**5.06**	**2.94**	**2.16**	**3.94**	**-0.63**	**-7.10**	**39.20**
	SD	**2.040**	**1.939**	**3.076**	**2.212**	**2.642**	**5.950**	**4.456**	**3.062**	**2.771**	**5.558**	**9.407**	**6.858**	**9.015**	**9.847**
	05-071	6.74	6.90	4.76	1.25	3.75	4.00	5.95	5.88	2.38	2.27	7.78	-4.82	-5.26	41.58
8 mg/kg	05-074	0	12.35	7.50	2.63	7.69	5.06	2.60	1.41	2.78	2.56	4.23	-4.23	-10.42	34.16
	05-075	4.76	11.11	5.19	1.28	6.76	2.67	2.70	4.41	2.78	2.56	5.41	4.17	-30.23	23.57
	05-085	4.94	7.50	13.10	1.30	2.54	10.98	14.61	13.33	14.02	11.88	1.09	-4.17	-12.28	78.83
	05-086	7.32	10.59	8.43	5.88	3.61	5.68	5.88	2.63	8.43	6.82	16.67	6.86	-20.31	68.50
	05-092	4.65	11.24	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-102	8.05	7.41	5.56	2.63	10.71	0	4.76	3.85	2.44	8.33	-1.25	3.53	-6.78	49.23
	05-106	5.56	10.11	6.74	3.37	3.45	5.56	1.20	4.71	5.49	3.30	2.27	1.20	-3.13	49.84
	05-108	6.82	5.68	6.90	1.27	8.33	17.02	17.86	2.83	5.56	5.00	2.11	0	-1.41	77.96
	05-112	5.88	8.89	6.74	3.30	7.61	5.62	12.00	8.24	7.29	4.85	13.73	1.04	8.24	93.42
	Mean	**5.47**	**9.18**	**7.21**	**2.55**	**6.05**	**6.29**	**7.51**	**5.25**	**5.69**	**5.29**	**5.78**	**0.40**	**-9.06**	**57.46**
	SD	**2.237**	**2.219**	**2.489**	**1.535**	**2.804**	**4.974**	**5.887**	**3.624**	**3.841**	**3.226**	**5.973**	**4.130**	**11.178**	**23.348**
	05-073	7.50	10.84	4.82	2.53	-1.30	10.39	5.00	9.59	5.68	13.64	12.63	8.16	7.50	96.99
10 mg/kg	05-083	1.25	9.20	6.82	3.66	5.88	5.75	-1.23	3.80	3.80	-3.75	6.49	-2.63	-1.82	37.21
	05-091	2.67	8.97	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-109	5.00	10.34	8.60	-2.35	5.62	8.70	6.52	-2.30	5.62	2.27	4.60	3.26	-13.11	42.77
	05-110	2.50	7.14	6.82	2.38	6.59	6.67	3.49	9.30	5.81	6.80	12.24	-6.74	3.90	66.90
	05-111	7.50	9.88	8.05	-1.33	2.56	10.47	10.59	20.59	3.88	8.33	(f)	(f)	(f)	(f)
	05-117	8.14	4.88	8.79	1.16	7.06	7.06	-1.14	7.95	8.33	6.67	5.62	2.13	7.46	74.12
	05-130	2.22	11.11	13.40	5.32	-5.06	8.60	14.77	3.66	-4.12	14.13	7.59	4.65	-9.52	66.75
	05-131	6.90	5.62	2.47	4.76	4.71	4.76	1.23	6.49	13.10	4.30	8.89	0	7.04	70.27
	05-132	5.00	11.83	9.52	4.44	15.00	15.60	9.57	10.53	5.36	0.91	1.89	10.78	-13.24	87.19
	Mean	**4.87**	**8.98**	**7.70**	**2.29**	**4.56**	**8.66**	**5.42**	**7.73**	**5.27**	**5.92**	**7.49**	**2.45**	**-1.47**	**67.77**
	SD	**2.566**	**2.365**	**3.066**	**2.688**	**5.626**	**3.252**	**5.491**	**6.258**	**4.521**	**5.795**	**3.689**	**5.657**	**9.262**	**20.137**
	05-080	-4.23	17.24	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
12 mg/kg	05-082	-1.37	16.25	8.24	7.14	4.71	7.06	9.88	8.05	15.96	13.16	8.41	2.00	-4.05	95.42
	05-087	3.80	7.50	7.23	7.06	10.87	9.18	9.68	4.60	2.22	16.19	-2.06	0	6.35	82.61
	05-096	2.53	14.63	3.75	2.47	8.05	-9.41	24.72	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-121	2.78	9.52	5.26	10.71	8.89	6.17	21.60	9.17	14.40	1.82	4.50	-2.08	-12.70	80.05
	05-122	6.49	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-123	8.54	9.47	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-124	2.74	12.94	8.70	6.67	9.38	10.42	10.00	6.38	-3.41	2.17	6.82	2.44	1.54	76.78
	05-128	2.53	12.05	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-134	7.23	12.77	2.20	5.26	4.55	2.17	7.69	9.52	5.95	10.00	1.10	7.61	-14.29	61.77
	Mean	**3.10**	**12.49**	**5.90**	**6.55**	**7.74**	**4.27**	**13.93**	**7.54**	**7.02**	**8.67**	**3.75**	**1.99**	**-4.63**	**79.32**
	SD	**3.846**	**3.252**	**2.599**	**2.693**	**2.580**	**7.279**	**7.268**	**2.051**	**8.174**	**6.473**	**4.258**	**3.617**	**8.906**	**12.095**
	05-093	4.17	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
15 mg/kg	05-097	6.67	4.94	5.19	8.00	5.88	19.57	15.38	-3.70	13.04	3.30	2.63	2.50	-4.69	78.71
	05-099	8.11	12.94	6.41	15.96	6.73	8.82	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-104	0	14.63	9.76	15.63	12.75	14.55	7.14	-3.19	1.11	10.00	-1.19	8.42	-15.00	74.60
	05-107	-1.54	13.25	2.63	23.15	14.78	17.95	9.17	8.66	-1.71	3.00	5.61	-1.00	-4.11	89.84
	05-113	6.98	13.19	14.91	19.20	10.66	4.69	9.82	6.78	3.97	5.93	6.45	2.52	-5.48	99.61
	05-116	-2.99	8.97	15.91	13.48	14.00	15.09	10.17	-8.70	10.28	19.30	1.87	-8.43	-7.02	81.95
	05-126	0	15.48	9.09	10.42	5.62	7.07	7.22	6.67	2.60	(f)	(f)	(f)	(f)	(f)
	05-129	8.75	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-133	0	15.29	8.79	8.33	3.57	4.60	14.61	7.95	2.13	-1.14	14.43	4.65	-6.78	76.44
	Mean	**3.01**	**12.34**	**9.09**	**14.27**	**9.25**	**11.54**	**10.50**	**2.07**	**4.49**	**6.73**	**4.97**	**1.44**	**-7.18**	**83.53**
	SD	**4.387**	**3.622**	**4.551**	**5.316**	**4.318**	**5.972**	**3.295**	**7.051**	**5.260**	**7.168**	**5.389**	**5.741**	**3.997**	**9.531**

= no data
(f) = Animal died on study

APPENDIX Q

SUMMARY OF 90-DAY BODY WEIGHT GAINS AND INDIVIDUAL BODY WEIGHT GAIN DATA

Appendix Q
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Summary of 90-Day Body Weight Gains

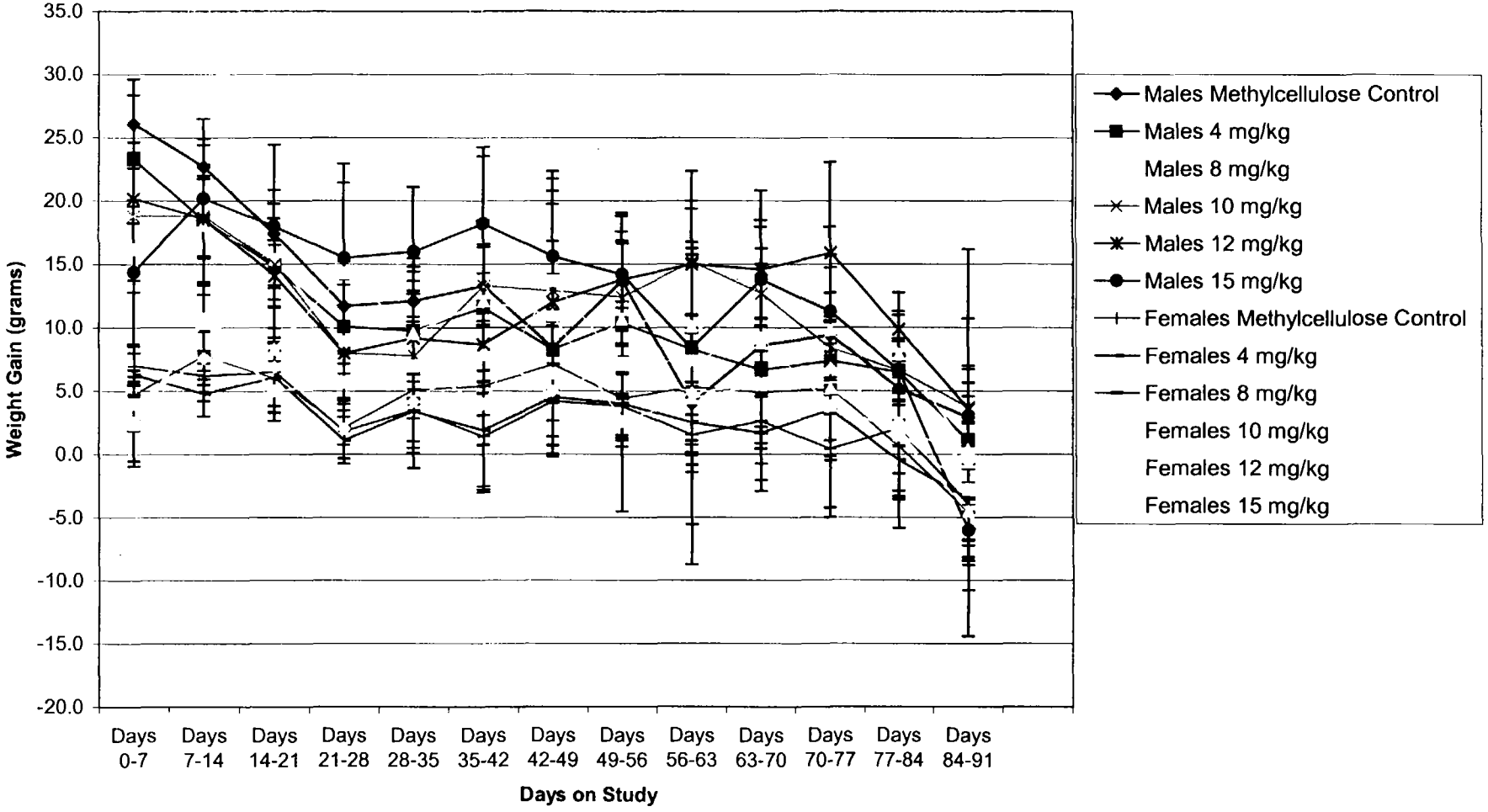


Table Q-1
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Summary of Body Weight Gains (grams)
Male Rats

Period		Methylcellulose Control	RDX in 1% Methylcellulose / 0.2% Tween 80				
			4 mg/kg	8 mg/kg	10 mg/kg	12 mg/kg	15 mg/kg
Days 0-7	Mean	26.1	23.3	16.2*	18.8*	20.2*	14.4*
	S.D.	3.51	5.06	3.39	5.05	4.44	5.70
	N	10	10	10	10	10	10
Days 7-14	Mean	22.7	18.5	18.1	18.8	18.6	20.2
	S.D.	3.77	5.89	4.77	3.16	3.13	4.71
	N	10	10	10	10	10	10
Days 14-21	Mean	17.4	14.8	15.4	15.0	14.1	18.0
	S.D.	2.37	6.05	3.20	1.89	2.42	6.43
	N	10	10	10	10	10	10
Days 21-28	Mean	11.7	10.1	8.9	8.0	8.0	15.5
	S.D.	3.53	3.73	4.48	3.77	5.89	7.43
	N	10	10	10	10	9	10
Days 28-35	Mean	12.1	9.8	9.5	7.8	9.2	16.0
	S.D.	1.60	3.12	3.17	7.69	5.24	5.12
	N	10	10	10	9	9	10
Days 35-42	Mean	13.3	11.6	8.4	13.3	8.7	18.2
	S.D.	3.06	4.97	3.57	10.23	5.61	6.05
	N	10	10	10	9	9	10
Days 42-49	Mean	8.4	8.3	6.4	12.9	12.0	15.6
	S.D.	5.78	8.51	5.02	8.85	7.73	5.17
	N	10	10	10	9	9	10
Days 49-56	Mean	13.7	10.4	10.7	12.4	13.8	14.2
	S.D.	5.10	1.65	5.93	5.17	5.24	2.64
	N	10	10	10	9	9	9
Days 56-63	Mean	4.0	8.3	10.1	15.2*	15.0*	8.4
	S.D.	12.74	2.63	5.65	4.18	5.02	13.97
	N	10	10	10	9	9	9
Days 63-70	Mean	8.6	6.7	8.8	12.7	14.6*	13.8*
	S.D.	9.35	1.89	6.23	8.14	3.89	4.71
	N	10	10	10	9	9	9
Days 70-77	Mean	9.4	7.4	9.8	8.4	15.9	11.3
	S.D.	3.34	1.96	4.92	7.33	7.16	6.65
	N	10	10	10	8	8	8
Days 77-84	Mean	5.2	6.5	7.9	6.6	9.9	6.6
	S.D.	2.53	2.64	3.10	4.69	2.85	2.33
	N	10	10	10	8	8	8
Days 84-91	Mean	2.9	1.1	0.4	3.7	3.6	-6.0
	S.D.	4.09	3.48	6.31	12.49	7.13	8.43
	N	10	10	9	7	8	7

* p less than or equal to 0.05
ANOVA with Holm-Sidak Method

Table Q-2
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Summary of Body Weight Gains (grams)
Female Rats

Period		Methylcellulose Control	RDX in 1% Methylcellulose / 0.2% Tween 80				
			4 mg/kg	8 mg/kg	10 mg/kg	12 mg/kg	15 mg/kg
Days 0-7	Mean	7.0	6.3	4.7	4.0*	2.5*	2.4*
	S.D.	1.56	1.70	1.95	2.16	3.03	3.37
	N	10	10	10	10	10	10
Days 7-14	Mean	6.2	4.8	7.8	7.6	10.7*	10.4*
	S.D.	1.99	1.81	1.87	2.12	2.74	3.20
	N	10	10	10	10	9	8
Days 14-21	Mean	6.5	6.1	6.0	6.9	5.0	8.3
	S.D.	2.72	2.77	2.18	3.06	2.37	5.04
	N	10	10	9	9	6	8
Days 21-28	Mean	1.8	1.1	2.1	2.0	5.7	14.3*
	S.D.	2.15	1.85	1.36	2.35	2.25	7.13
	N	10	10	9	9	6	8
Days 28-35	Mean	3.5	3.4	5.1	4.2	7.0	9.6*
	S.D.	2.99	2.37	2.26	5.29	2.53	5.21
	N	10	10	9	9	6	8
Days 35-42	Mean	1.4	1.9	5.4	7.9*	4.0	12.1*
	S.D.	4.43	4.72	4.67	3.79	6.54	6.36
	N	10	10	9	9	6	8
Days 42-49	Mean	4.2	4.5	7.1	5.0	13.7*	11.0*
	S.D.	4.21	3.78	6.45	5.12	8.64	3.21
	N	10	10	9	9	6	7
Days 49-56	Mean	3.8	4.0	4.4	7.1	7.2	2.6
	S.D.	2.53	2.49	3.32	6.51	2.59	7.14
	N	10	10	9	9	5	7
Days 56-63	Mean	1.5	2.5	5.3	4.8	7.4	4.4
	S.D.	1.58	2.37	4.24	4.06	8.85	5.26
	N	10	10	9	9	5	7
Days 63-70	Mean	2.6	1.7	4.9	5.6	9.2	5.5
	S.D.	4.67	4.64	3.26	5.17	7.05	4.64
	N	10	10	9	9	5	6
Days 70-77	Mean	0.4	3.5	5.2	6.8	3.8	5.2
	S.D.	5.40	7.74	5.70	3.65	4.32	5.38
	N	10	10	9	8	5	6
Days 77-84	Mean	2.0	-0.5	0.6	2.5	1.8	1.5
	S.D.	5.35	5.36	3.54	5.40	3.35	5.09
	N	10	10	9	8	5	6
Days 84-91	Mean	-4.0	-3.5	-4.6	-0.6	-2.8	-4.5
	S.D.	3.23	4.95	6.17	6.25	5.36	2.26
	N	10	10	9	8	5	6

* p less than or equal to 0.05
ANOVA with Holm-Sidak Method

Table Q-3
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

90-Day Individual Body Weight Gains (grams)
Male Rats

Group	Animal ID	Days 0-7	Days 7-14	Days 14-21	Days 21-28	Days 28-35	Days 35-42	Days 42-49	Days 49-56	Days 56-63	Days 63-70	Days 70-77	Days 77-84	Days 84-91	Net Change
Methylcellulose Control	05-011	26	30	16	16	13	11	9	15	5	9	12	1	10	173
	05-012	28	23	14	15	13	14	8	12	9	6	12	2	1	164
	05-016	30	22	19	12	13	15	10	9	5	3	6	7	2	153
	05-020	30	25	20	5	13	7	-5	26	-31	34	7	8	8	150
	05-023	25	24	21	9	12	16	11	15	7	5	8	4	2	159
	05-052	24	22	15	11	8	12	6	14	3	4	8	4	2	133
	05-060	25	23	18	14	12	15	17	10	12	12	11	8	4	181
	05-064	28	24	19	15	13	12	11	8	6	3	16	5	-4	161
	05-066	18	17	17	12	13	13	5	16	13	5	5	8	5	147
	05-070	27	17	15	8	11	18	12	12	11	5	9	5	-1	149
	Mean	**26.1**	**22.7**	**17.4**	**11.7**	**12.1**	**13.3**	**8.4**	**13.7**	**4.0**	**8.6**	**9.4**	**5.2**	**2.9**	**157.0**
	SD	**3.51**	**3.77**	**2.37**	**3.53**	**1.60**	**3.06**	**5.78**	**5.10**	**12.74**	**9.35**	**3.34**	**2.53**	**4.09**	**13.77**
4 mg/kg	05-001	21	13	17	8	16	17	1	13	9	7	4	4	4	134
	05-007	28	15	18	14	8	1	31	11	11	5	9	9	0	167
	05-013	16	14	7	9	7	8	1	10	6	4	6	6	2	96
	05-028	27	21	12	4	8	17	9	12	4	9	7	4	-5	135
	05-033	24	13	3	14	9	12	7	10	7	8	9	6	0	122
	05-039	29	19	20	11	14	11	9	10	10	9	10	3	0	159
	05-041	22	23	16	15	7	16	5	11	9	7	8	7	5	151
	05-055	26	24	23	11	12	14	9	7	13	8	9	7	-1	151
	05-062	26	30	18	10	9	12	6	9	7	6	7	12	-1	151
	05-067	14	13	14	5	8	8	5	11	7	4	5	7	7	110
	Mean	**23.3**	**18.5**	**14.8**	**10.1**	**9.8**	**11.6**	**8.3**	**10.4**	**8.3**	**6.7**	**7.4**	**6.5**	**1.1**	**137.6**
	SD	**5.06**	**5.89**	**6.05**	**3.73**	**3.12**	**4.97**	**8.51**	**1.65**	**2.63**	**1.89**	**1.96**	**2.64**	**3.48**	**22.65**
8 mg/kg	05-003	13	8	13	3	7	4	4	12	3	11	5	11	2	96
	05-006	12	18	17	5	4	8	7	8	7	10	5	6	13	124
	05-015	12	13	9	1	9	7	0	7	6	3	8	10	-5	80
	05-034	20	16	14	12	13	9	0	24	12	16	18	10	-7	164
	05-037	18	20	18	10	12	4	7	11	12	8	7	11	-6	132
	05-045	13	22	19	8	14	9	1	11	24	20	19	(f)	(f)	160
	05-046	20	18	15	14	9	10	14	17	7	11	8	5	5	153
	05-051	16	22	19	12	11	16	9	6	10	6	11	2	2	147
	05-068	19	20	13	13	10	11	10	5	10	4	8	7	-2	128
	05-069	19	24	17	11	6	6	12	6	10	-1	9	9	2	130
	Mean	**16.2**	**18.1**	**15.4**	**8.9**	**9.5**	**8.4**	**6.4**	**10.7**	**10.1**	**8.8**	**9.8**	**7.9**	**0.4**	**131.4**
	SD	**3.39**	**4.77**	**3.20**	**4.48**	**3.17**	**3.57**	**5.02**	**5.93**	**5.65**	**6.23**	**4.92**	**3.10**	**6.31**	**26.99**
10 mg/kg	05-017	20	21	17	3	13	20	27	21	13	-4	(f)	(f)	(f)	151
	05-024	13	24	15	9	15	10	6	8	12	8	1	6	-21	108
	05-040	21	16	13	4	5	10	17	17	14	21	6	13	11	168
	05-042	13	20	16	6	10	17	21	11	23	12	15	1	0	172
	05-049	11	15	16	9	11	7	3	6	15	14	9	11	6	133
	05-050	21	22	17	13	12	5	4	8	9	8	7	11	3	144
	05-053	19	14	12	8	8	5	4	10	16	14	10	7	19	146
	05-054	26	19	17	14	-11	37	19	13	20	23	-2	2	--	177
	05-056	25	18	14	4	--	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	61
	05-065	19	19	13	10	7	9	15	18	15	18	21	2	8	177
	Mean	**18.8**	**18.8**	**15.0**	**8.0**	**7.8**	**13.3**	**12.9**	**12.4**	**15.2**	**12.7**	**8.4**	**6.6**	**3.7**	**143.7**
	SD	**5.05**	**3.16**	**1.89**	**3.77**	**7.69**	**10.23**	**8.85**	**5.17**	**4.18**	**8.14**	**7.33**	**4.69**	**12.49**	**36.36**
12 mg/kg	05-005	20	17	14	8	13	8	23	10	20	18	23	9	-2	181
	05-009	21	14	14	6	2	5	9	19	7	14	9	7	8	141
	05-019	24	19	10	21	17	17	3	14	23	(f)	(f)	(f)	(f)	148
	05-021	21	19	17	6	9	4	10	16	10	18	15	15	-6	164
	05-027	23	16	16	6	4	9	17	6	14	18	11	10	10	160
	05-031	14	15	11	0	6	2	10	20	12	8	23	11	8	147
	05-047	13	21	12	4	5	5	0	13	14	14	24	9	11	145
	05-048	16	23	17	9	13	10	15	19	18	17	17	6	-6	180
	05-058	25	23	15	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	63
	05-063	25	19	15	12	14	18	21	7	17	10	5	12	6	185
	Mean	**20.2**	**18.6**	**14.1**	**8.0**	**9.2**	**8.7**	**12.0**	**13.8**	**15.0**	**14.6**	**15.9**	**9.9**	**3.6**	**151.4**
	SD	**4.44**	**3.13**	**2.42**	**5.89**	**5.24**	**5.61**	**7.73**	**5.24**	**5.02**	**3.89**	**7.16**	**2.85**	**7.13**	**35.84**
15 mg/kg	05-008	11	27	31	17	22	25	18	15	-21	(f)	(f)	(f)	(f)	145
	05-010	24	17	12	13	19	9	24	17	5	18	5	8	--	171
	05-018	6	14	11	20	8	17	7	14	27	12	7	5	-5	143
	05-022	16	22	13	20	18	16	12	16	0	13	5	7	-8	155
	05-025	20	15	21	24	20	25	19	(f)	(f)	(f)	(f)	(f)	(f)	144
	05-030	8	21	18	16	21	19	11	16	4	9	15	4	1	174
	05-032	10	18	19	6	8	22	11	11	14	11	6	7	0	143
	05-035	19	18	23	1	15	10	20	17	21	8	23	7	-10	179
	05-043	14	22	21	14	12	14	17	10	10	18	17	11	2	182
	05-057	16	28	11	24	17	25	17	12	16	21	12	4	-22	166
	Mean	**14.4**	**20.2**	**18.0**	**15.5**	**16.0**	**18.2**	**15.6**	**14.2**	**8.4**	**13.8**	**11.3**	**6.6**	**-6.0**	**160.2**
	SD	**5.70**	**4.71**	**6.43**	**7.43**	**5.12**	**6.85**	**5.17**	**2.64**	**13.97**	**4.71**	**6.65**	**2.33**	**8.43**	**15.92**

(f) = Animal died on study

Table Q-4
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

90-Day Individual Body Weight Changes (grams)
Female Rats

	Animal ID	Days 0-7	Days 7-14	Days 14-21	Days 21-28	Days 28-35	Days 35-42	Days 42-49	Days 49-56	Days 56-63	Days 63-70	Days 70-77	Days 77-84	Days 84-90	Net Change
Methylcellulose Control	05-076	7	7	6	1	10	3	1	4	2	6	-1	1	-4	43
	05-077	8	2	5	4	1	3	4	2	3	6	-13	13	-4	38
	05-084	8	7	6	-1	3	3	3	2	1	2	8	-2	-4	36
	05-088	4	5	6	1	3	3	3	2	4	-9	0	8	1	31
	05-098	8	7	3	5	1	3	6	4	0	1	1	5	-6	38
	05-100	5	8	7	2	4	-11	14	6	2	2	4	-4	-7	37
	05-101	9	5	12	0	7	1	2	9	1	5	0	0	-6	45
	05-114	7	9	3	-1	1	3	-2	6	0	3	3	3	-8	29
	05-120	6	5	9	3	4	2	6	2	-1	8	2	-1	-4	41
	05-127	8	7	8	4	1	4	5	1	3	2	0	-3	2	41
	Mean	7.0	6.2	6.5	1.8	3.5	1.4	4.2	3.8	1.5	2.6	0.4	2.0	-4.0	37.9
	SD	1.56	1.99	2.72	2.15	2.99	4.43	4.21	2.53	1.58	4.67	5.40	5.35	3.23	5.02
4 mg/kg	05-072	9	1	1	-2	3	6	0	6	0	4	13	-7	-5	29
	05-078	5	6	9	0	5	3	2	4	1	2	3	-1	-1	41
	05-081	9	4	8	0	1	4	4	4	5	2	8	-4	-3	42
	05-090	7	8	7	1	6	2	2	0	6	-9	15	-2	-12	34
	05-094	6	5	4	0	2	5	5	2	1	5	2	-2	-3	32
	05-095	5	6	7	2	3	-11	14	9	2	1	-11	13	-4	38
	05-105	5	5	8	4	8	2	3	3	-1	7	4	-2	-5	41
	05-115	6	5	7	1	1	2	6	2	5	3	-1	1	-8	36
	05-135	7	4	8	4	1	3	4	5	4	-3	6	-3	7	47
	05-136	4	4	2	1	4	3	5	5	2	5	-4	2	-1	32
	Mean	6.3	4.8	6.1	1.1	3.4	1.9	4.5	4.0	2.5	1.7	3.5	-0.5	-3.5	37.2
	SD	1.70	1.81	2.77	1.85	2.37	4.72	3.78	2.49	2.37	4.64	7.74	5.36	4.95	5.59
8 mg/kg	05-071	6	6	4	1	3	3	5	5	2	2	7	-4	-3	37
	05-074	0	10	6	2	6	4	2	1	2	2	3	-3	-5	33
	05-075	4	9	4	1	5	2	2	3	2	2	4	3	-13	28
	05-085	4	6	11	1	3	9	13	12	15	12	1	-3	-7	83
	05-086	6	9	7	5	3	5	5	2	7	6	15	7	-13	64
	05-092	4	10	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	14
	05-102	7	6	4	2	9	0	4	3	2	7	-1	3	-4	42
	05-106	5	9	6	3	3	5	1	4	5	3	2	1	-2	47
	05-108	6	5	6	1	7	16	20	3	6	5	2	0	-1	76
	05-112	5	8	6	3	7	5	12	7	7	5	14	1	7	88
	Mean	4.7	7.8	6.0	2.1	5.1	5.4	7.1	4.4	5.3	4.9	5.2	0.6	-4.6	51.2
	SD	1.95	1.87	2.18	1.36	2.26	4.67	6.45	3.32	4.24	3.26	5.70	3.54	6.17	25.17
10 mg/kg	05-073	6	9	4	2	-1	8	4	7	5	12	12	8	6	82
	05-083	1	8	6	3	5	5	-1	3	3	-3	5	-2	-1	34
	05-091	2	7	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	9
	05-109	4	9	8	-2	5	8	6	-2	5	2	4	3	-8	50
	05-110	2	6	6	2	6	6	3	8	5	7	12	-6	3	60
	05-111	6	8	7	-1	2	9	9	21	4	8	(f)	(f)	(f)	73
	05-117	7	4	8	1	6	6	-1	7	8	6	5	2	5	64
	05-130	2	9	13	5	-4	8	13	3	-4	13	6	4	-6	72
	05-131	6	5	2	4	4	4	1	5	11	4	8	0	5	59
	05-132	4	11	8	4	15	17	11	12	6	1	2	11	-9	100
	Mean	4.0	7.6	6.9	2.0	4.2	7.9	5.0	7.1	4.8	5.6	6.8	2.5	-0.6	60.3
	SD	2.16	2.12	3.06	2.35	5.29	3.79	5.12	6.51	4.06	5.17	3.65	5.40	6.25	25.36
12 mg/kg	05-080	-3	15	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	12
	05-082	-1	13	7	6	4	6	8	7	15	15	9	2	-3	92
	05-087	3	6	6	6	10	9	9	4	2	17	-2	0	4	74
	05-096	2	12	3	2	7	-8	22	(f)	(f)	(f)	(f)	(f)	(f)	40
	05-121	2	8	4	9	8	5	27	11	18	2	5	-2	-8	89
	05-122	5	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	5
	05-123	7	9	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	16
	05-124	2	11	8	6	9	10	10	6	-3	2	6	2	1	71
	05-128	2	10	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	12
	05-134	6	12	2	5	4	2	6	8	5	10	1	7	-8	60
	Mean	2.5	10.7	5.0	5.7	7.0	4.0	13.7	7.2	7.4	9.2	3.8	1.8	-2.8	47.1
	SD	3.03	2.74	2.37	2.25	2.53	6.54	8.64	2.59	8.85	7.05	4.32	3.35	5.36	34.14
15 mg/kg	05-093	3	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	3
	05-097	5	4	4	6	5	18	16	-3	12	3	2	2	-3	71
	05-099	6	11	5	15	7	9	(f)	(f)	(f)	(f)	(f)	(f)	(f)	53
	05-104	0	12	8	15	13	16	7	-3	1	10	-1	8	-9	79
	05-107	-1	11	2	25	17	21	11	11	-2	3	6	-1	-3	100
	05-113	6	12	17	24	13	6	11	8	5	7	8	3	-4	119
	05-116	-2	7	14	12	14	16	12	-8	11	11	2	-7	-4	78
	05-126	0	13	8	10	5	7	7	6	2	(f)	(f)	(f)	(f)	58
	05-129	7	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	7
	05-133	0	13	8	7	3	4	13	7	2	-1	14	4	-4	70
	Mean	2.4	10.4	8.3	14.3	9.6	12.1	11.0	2.6	4.4	5.5	5.2	1.5	-4.5	63.8
	SD	3.37	3.20	5.04	7.13	5.21	6.36	3.21	7.14	5.26	4.64	5.38	5.09	2.26	36.44

APPENDIX R

SUMMARY OF 90-DAY ORGAN WEIGHTS AND INDIVIDUAL ORGAN WEIGHT DATA

Table R-1
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Summary of Organ Weights
Male Rats

Absolute Organ Weight (grams)

Period		Methylcellulose Control	RDX in 1% Methylcellulose / 0.2% Tween 80				
			4 mg/kg	8 mg/kg	10 mg/kg	12 mg/kg	15 mg/kg
Body Weight	Mean	319.0	299.9	291.0	310.3	325.8	326.6
	S.D.	14.12	26.92	25.95	30.02	19.51	13.20
	N	10	10	9	7	8	7
Adrenals	Mean	0.0472	0.0479	0.0475	0.0508	0.0478	0.0560
	S.D.	0.00587	0.01532	0.00359	0.00621	0.00501	0.01050
	N	9	10	8	6	8	7
Brain	Mean	1.9279	1.9078	1.9224	1.9669	2.0313*	2.0566*
	S.D.	0.06487	0.07691	0.07071	0.07835	0.06751	0.06973
	N	10	10	9	7	8	7
Heart	Mean	0.9329	0.9140	0.8660	0.9197	0.9459	1.0341
	S.D.	0.04538	0.09166	0.08058	0.09535	0.06163	0.24039
	N	10	10	9	7	8	7
Kidneys	Mean	1.9827	1.9192	1.9058	1.9647	2.0354	2.0817
	S.D.	0.13066	0.15142	0.16887	0.19099	0.14189	0.15248
	N	10	10	9	7	8	7
Liver	Mean	11.9557	11.2884	10.8270	11.9090	12.7635	12.5249
	S.D.	0.96047	1.55158	1.40739	1.92988	0.81709	0.85244
	N	10	10	9	7	8	7
Spleen	Mean	0.6929	0.6704	0.6538	0.7149	0.6995	0.7256
	S.D.	0.03863	0.04731	0.05164	0.05621	0.03571	0.11023
	N	10	10	9	7	8	7
Testes	Mean	1.0140	1.0522	1.0608	1.0083	0.9532	0.9145
	S.D.	0.05454	0.04645	0.05918	0.11632	0.06624	0.04569
	N	10	10	9	7	8	7
Thymus	Mean	0.0749	0.0740	0.0768	0.0675	0.0661	0.0565
	S.D.	0.02253	0.02695	0.02315	0.01488	0.01121	0.00975
	N	10	10	9	7	8	7
Epididymides	Mean	0.3412	0.3603	0.3442	0.3385	0.3198	0.3107
	S.D.	0.02199	0.02643	0.02176	0.02687	0.03115	0.03010
	N	10	10	9	7	8	7

* p less than or equal to 0.05
ANOVA with Holm-Sidak Method

Table R-2
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Summary of Organ Weights
Female Rats

Absolute Organ Weight (grams)

Period		Methylcellulose Control	RDX in 1% Methylcellulose / 0.2% Tween 80				
			4 mg/kg	8 mg/kg	10 mg/kg	12 mg/kg	15 mg/kg
Body Weight	Mean	176.6	176.1	191.9	204.3*	208.8*	221.7*
	S.D.	6.83	7.05	23.71	18.20	12.52	21.65
	N	10	10	9	8	5	6
Adrenals	Mean	0.0638	0.0661	0.0634	0.0708	0.0656	0.0686
	S.D.	0.00607	0.00640	0.01354	0.01177	0.01658	0.00907
	N	10	10	9	8	5	5
Brain	Mean	1.7493.	1.7184	1.8488	1.7674	1.8188	1.8575
	S.D.	0.06331	0.09535	0.10849	0.09335	0.08862	0.03919
	N	10	10	9	8	5	6
Heart	Mean	0.6219	0.6089	0.6240	0.6735	0.6674	0.6568
	S.D.	0.05206	0.04366	0.06411	0.03787	0.06113	0.11428
	N	10	10	9	8	5	6
Kidneys	Mean	1.2596	1.2756	1.3197	1.4213*	1.3898	1.4485*
	S.D.	0.08021	0.07318	0.10498	0.05893	0.10124	0.07357
	N	10	10	9	8	5	6
Liver	Mean	6.1214	6.1575	6.5228	7.2055*	7.0500	7.8243*
	S.D.	0.65393	0.50939	1.04163	0.92069	0.72726	1.12979
	N	10	10	9	8	5	6
Spleen	Mean	0.4467	0.4492	0.4821	0.5498*	0.5240*	0.5533*
	S.D.	0.02846	0.03130	0.06208	0.05023	0.01867	0.08282
	N	10	10	9	8	5	6
Ovaries	Mean	0.1223	0.1170	0.1250	0.1336	0.1412	0.1292
	S.D.	0.01966	0.01457	0.02230	0.01433	0.01873	0.01668
	N	10	10	9	8	5	6
Thymus	Mean	0.1934	0.1789	0.2173	0.2304	0.2556	0.2300
	S.D.	0.05175	0.04907	0.02646	0.05968	0.03553	0.07240
	N	10	10	9	8	5	6
Uterus	Mean	0.5671	0.6533	0.5333	0.5796	0.3928	0.4608
	S.D.	0.21722	0.36763	0.22888	0.22415	0.13133	0.12719
	N	10	10	9	8	5	6

* p less than or equal to 0.05
ANOVA with Holm-Sidak Method

Table R-3
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Summary of Organ Weights
Male Rats

% Body Weight

Period		Methylcellulose Control	RDX in 1% Methylcellulose / 0.2% Tween 80				
			4 mg/kg	8 mg/kg	10 mg/kg	12 mg/kg	15 mg/kg
Adrenals	Mean	0.0149	0.0158	0.0166	0.0166	0.0147	0.0171
	S.D.	0.00162	0.00456	0.00104	0.00118	0.00185	0.00310
	N	9	10	8	6	8	7
Brain	Mean	0.6056	0.6394	0.6638	0.6382	0.6252	0.6303
	S.D.	0.03713	0.04386	0.04192	0.05644	0.03575	0.02330
	N	10	10	9	7	8	7
Heart	Mean	0.2928	0.3048	0.2980	0.2967	0.2905	0.3166
	S.D.	0.01633	0.01570	0.01768	0.01674	0.01268	0.07018
	N	10	10	9	7	8	7
Kidneys	Mean	0.6215	0.6409	0.6552	0.6332	0.6251	0.6376
	S.D.	0.02943	0.02331	0.01898	0.01090	0.03022	0.04187
	N	10	10	9	7	8	7
Liver	Mean	3.7455	3.7500	3.7100	3.8181	3.9193	3.8341
	S.D.	0.21911	0.20334	0.19831	0.34748	0.13440	0.18039
	N	10	10	9	7	8	7
Spleen	Mean	0.2173	0.2243	0.2253	0.2324	0.2153	0.2218
	S.D.	0.01051	0.01439	0.01468	0.02976	0.01555	0.02891
	N	10	10	9	7	8	7
Testes	Mean	1.0140	1.0522	1.0608	1.0083	0.9532	0.9145*
	S.D.	0.05454	0.04645	0.05918	0.11632	0.06624	0.04569
	N	10	10	9	7	8	7
Thymus	Mean	0.0749	0.0740	0.0768	0.0675	0.0661	0.0565
	S.D.	0.02253	0.02695	0.02315	0.01488	0.01121	0.00975
	N	10	10	9	7	8	7
Epididymides	Mean	0.3412	0.3603	0.3442	0.3385	0.3198	0.3107
	S.D.	0.02199	0.02643	0.02176	0.02687	0.03115	0.03010
	N	10	10	9	7	8	7

* p less than or equal to 0.05
ANOVA with Holm-Sidak Method

Table R-4
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Summary of Organ Weights
Female Rats

% Body Weight

Period		Methylcellulose Control	RDX in 1% Methylcellulose / 0.2% Tween 80				
			4 mg/kg	8 mg/kg	10 mg/kg	12 mg/kg	15 mg/kg
Adrenals	Mean	0.0362	0.0376	0.0333	0.0349	0.0312	0.0306
	S.D.	0.00409	0.00366	0.00731	0.00634	0.00700	0.00458
	N	10	10	9	8	5	5
Brain	Mean	0.9920	0.9759	0.9727	0.8723*	0.8724*	0.8431*
	S.D.	0.05688	0.04102	0.09459	0.09729	0.04587	0.06395
	N	10	10	9	8	5	6
Heart	Mean	0.3520	0.3458	0.3264	0.3308	0.3197	0.2959*
	S.D.	0.02435	0.02056	0.01885	0.01536	0.02262	0.03955
	N	10	10	9	8	5	6
Kidneys	Mean	0.7129	0.7246	0.6918	0.6990	0.6662	0.6561*
	S.D.	0.02815	0.03630	0.04676	0.04459	0.04004	0.03563
	N	10	10	9	8	5	6
Liver	Mean	3.4591	3.4936	3.3878	3.5212	3.3703	3.5183
	S.D.	0.26521	0.20852	0.18514	0.20579	0.16456	0.17869
	N	10	10	9	8	5	6
Spleen	Mean	0.2529	0.2551	0.2521	0.2693	0.2516	0.2487
	S.D.	0.01106	0.01517	0.02309	0.01309	0.01658	0.01524
	N	10	10	9	8	5	6
Ovaries	Mean	0.0694	0.0664	0.0655	0.0658	0.0676	0.0584
	S.D.	0.01149	0.00713	0.01040	0.00838	0.00773	0.00671
	N	10	10	9	8	5	6
Thymus	Mean	0.1095	0.1017	0.1143	0.1136	0.1224	0.1028
	S.D.	0.02943	0.02817	0.01659	0.03118	0.01525	0.04668
	N	10	10	9	8	5	6
Uterus	Mean	0.3207	0.3674	0.2801	0.2871	0.1875	0.2066
	S.D.	0.12145	0.19601	0.12376	0.12142	0.05915	0.04668
	N	10	10	9	8	5	6

* p less than or equal to 0.05
ANOVA with Holm-Sidak Method

Table R-5
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Summary of Organ Weights
Male Rats

% Brain Weight

Period		Methylcellulose Control	RDX in 1% Methylcellulose / 0.2% Tween 80				
			4 mg/kg	8 mg/kg	10 mg/kg	12 mg/kg	15 mg/kg
Adrenals	Mean	2.4552	2.4932	2.4860	2.6089	2.3545	2.7218
	S.D.	0.36521	0.75906	0.14765	0.26067	0.27165	0.49428
	N	9	10	8	6	8	7
Heart	Mean	48.4819	47.8937	45.0108	46.7090	46.5700	50.0664
	S.D.	3.55353	4.29763	3.40772	3.77389	2.67529	9.87856
	N	10	10	9	7	8	7
Kidneys	Mean	103.0378	100.5007	99.0024	99.8868	100.2072	101.1753
	S.D.	8.88590	5.05913	6.03623	8.97279	6.21810	5.82984
	N	10	10	9	7	8	7
Liver	Mean	621.7388	590.5503	562.1051	604.6061	628.2274	609.3125
	S.D.	65.17254	67.93971	60.61275	89.91823	31.75012	41.60433
	N	10	10	9	7	8	7
Spleen	Mean	35.9887	35.1060	34.0100	36.3681	34.4462	35.2077
	S.D.	2.53149	1.26915	2.46886	2.81723	1.58209	4.45521
	N	10	10	9	7	8	7
Testes	Mean	167.7570	164.8508	159.9684	157.8517*	152.5598*	145.2828*
	S.D.	9.73833	5.54034	6.06786	8.90849	8.04021	9.36411
	N	10	10	9	7	8	7
Thymus	Mean	12.4167	11.5730	11.6223	10.5086	10.5651	8.9811
	S.D.	3.71900	4.26137	3.56853	1.56165	1.70823	1.60723
	N	10	10	9	7	8	7
Epididymides	Mean	56.4552	56.4801	51.9116*	53.1624	51.185*	49.3021*
	S.D.	4.13050	4.54087	2.60019	3.35520	4.29055	4.50721
	N	10	10	9	7	8	7

* p less than or equal to 0.05
ANOVA with Holm-Sidak Method

Table R-6
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Summary of Organ Weights
Female Rats

% Brain Weight

Period		Methylcellulose Control	RDX in 1% Methylcellulose / 0.2% Tween 80				
			4 mg/kg	8 mg/kg	10 mg/kg	12 mg/kg	15 mg/kg
Adrenals	Mean	3.6487	3.8547	3.4261	4.0116	3.5858	3.6846
	S.D.	0.34309	0.41094	0.66393	0.66893	0.82663	0.50289
	N	10	10	9	8	5	5
Heart	Mean	35.6032	35.5257	33.8203	38.2296	36.7374	35.2988
	S.D.	3.26682	3.12133	3.71743	3.47546	3.42206	5.64455
	N	10	10	9	8	5	6
Kidneys	Mean	72.1427	74.3003	71.4756	80.6241*	76.5805	77.9613
	S.D.	5.86587	3.48329	5.41966	5.76446	6.95966	3.03952
	N	10	10	9	8	5	6
Liver	Mean	350.7983	358.7203	352.4425	410.0227	387.7889	420.5264*
	S.D.	42.45697	27.62053	50.28639	69.98630	36.83905	52.66803
	N	10	10	9	8	5	6
Ovaries	Mean	6.9962	6.8024	6.7911	7.6154	7.7732	6.9495
	S.D.	1.15678	0.69901	1.32119	1.25961	1.01480	0.83865
	N	10	10	9	8	5	6
Spleen	Mean	25.5467	26.1802	26.1354	31.2584*	28.8357	29.7377*
	S.D.	1.54030	1.88141	3.54948	4.18678	0.93083	3.89700
	N	10	10	9	8	5	6
Thymus	Mean	11.0482	10.3593	11.7766	13.1060	14.0034	12.3549
	S.D.	2.92382	2.65625	1.51030	3.60240	1.33043	3.71897
	N	10	10	9	8	5	6
Uterus	Mean	32.4798	37.8367	28.9092	33.0183	21.4959	24.7207
	S.D.	12.26092	20.79830	12.47726	13.27755	6.75169	6.35462
	N	10	10	9	8	5	6

* p less than or equal to 0.05
ANOVA with Holm-Sidak Method

Table R-7
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

90-Day Individual Organ Weights
Male Rats

ABSOLUTE ORGAN WEIGHTS (grams)

	Animal ID	Body Weight	Adrenals	Brain	Heart	Kidneys	Liver	Spleen	Testes	Thymus	Epididymides
Methylcellulose Control	05-011	341	0.046	1.945	0.927	1.993	12.615	0 769	3 379	0.190	1 127
	05-012	330		1.913	1.024	2.194	12.599	0 696	3 313	0.260	1.241
	05-016	316	0.045	1.993	0.875	1.901	10.877	0 701	3 224	0.278	1 071
	05-020	314	0.045	2.028	0.867	1.979	11.146	0 693	3.174	0 075	1 071
	05-023	319	0.056	1 830	0 936	2.068	13.075	0 732	3.370	0.181	1.031
	05-052	290	0.041	1.947	0.942	1.723	10.043	0.676	3 278	0.270	1 055
	05-060	334	0.057	1.869	0.974	2 019	12.341	0 707	3.362	0.308	1.111
	05-064	312	0.050	1 954	0 909	1 852	11.884	0 642	3.207	0.262	1 040
	05-066	313	0 043	1.839	0.945	2 061	12.522	0 669	2.880	0.283	0 953
	05-070	321	0 042	1.961	0.930	2 037	12.455	0.644	3 123	0 277	1.180
	Mean	**319.0**	**0.0472**	**1.9279**	**0.9329**	**1.9827**	**11.9557**	**0.6929**	**3.2310**	**0.2384**	**1.0880**
	SD	**14.12**	**0.00587**	**0.06487**	**0.04538**	**0.13066**	**0.9604725**	**0.03863**	**0.15131**	**0.07012**	**0.08122**
4 mg/kg	05-001	300	0 047	1 900	0.975	1 906	11.245	0 640	3.180	0.227	1.016
	05-007	343	0.052	2 001	0.974	2.162	13 788	0.699	3 382	0 326	1 336
	05-013	256	0.029	1.879	0 729	1.769	8.930	0 651	2 866	0 226	1.019
	05-028	306	0 065	1.961	0.920	1.903	11.787	0 704	3.223	0.153	1 192
	05-033	281	0 015	1 782	0 894	1.720	10.240	0 609	2.977	0.121	0.976
	05-039	314	0 055	1.957	0.947	2.005	11 662	0.716	3.217	0.316	1 173
	05-041	316	0 053	1.888	1.039	2 058	12.845	0 668	3.276	0.079	1 028
	05-055	315	0.063	1.928	0.919	1.947	12.208	0 701	3.173	0.304	1.036
	05-062	308	0 055	1.994	0.953	2.020	11.144	0.728	3.198	0.204	1.075
	05-067	260	0 045	1.788	0.790	1.702	9 035	0 588	2 956	0.260	0 943
	Mean	**299.9**	**0.0479**	**1.9078**	**0.9140**	**1.9192**	**11.2884**	**0.6704**	**3.1448**	**0.2216**	**1.0794**
	SD	**26.92**	**0.01532**	**0.07691**	**0.09166**	**0.15142**	**1.5515794**	**0.04731**	**0.16028**	**0.08406**	**0.11963**
8 mg/kg	05-003	253	0.041	1.825	0.741	1.592	8.579	0 552	2.721	0.105	0 892
	05-006	292	0 053	1 913	0.815	1.848	10.393	0.708	3.174	0.255	0 960
	05-015	251	0 045	1 826	0.758	1.727	9 196	0 617	2.858	0.272	0 934
	05-034	321		2.025	0 844	2.130	12 005	0 663	3 180	0.130	0 968
	05-037	297	0 049	1.906	0.910	1.931	11.474	0 657	3.125	0.245	1.059
	05-045	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-046	320	0.050	2.002	0 964	2.062	12.202	0.673	3.086	0.276	1.076
	05-051	313	0.048	1 935	0 945	2.035	12.710	0.699	3.236	0.306	1.040
	05-068	290	0 046	1 893	0 918	1.947	10 892	0.703	3.094	0.224	1.022
	05-069	282	0 048	1.977	0 899	1 880	9 992	0.612	3.210	0.196	1 031
	Mean	**291.0**	**0.0475**	**1.9224**	**0.8660**	**1.9058**	**10.8270**	**0.6538**	**3.0760**	**0.2232**	**0.9980**
	SD	**25.95**	**0.00359**	**0.07071**	**0.08058**	**0.16887**	**1.40739**	**0.05164**	**0.17333**	**0.06792**	**0.06216**
10 mg/kg	05-017	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-024	257	0.046	1.917	0.806	1.622	8 027	0.705	3.141	0.237	0.966
	05-040	333		2.096	0.988	2.069	12.720	0.716	2.940	0.216	0.990
	05-042	343	0.056	1.937	0.950	2.205	13.227	0.643	3.026	0.208	1.071
	05-049	294	0.046	1.954	0.817	1.843	11.487	0.759	3.079	0.247	1.059
	05-050	300	0 045	1.857	0.860	1.920	11.213	0.721	3.133	0.154	1.021
	05-053	310	0.052	1.973	0.953	2.012	13.123	0 655	3.104	0.192	1.044
	05-054	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-056	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-065	335	0 060	2.034	1.064	2.082	13.566	0.805	3.275	0.193	1 162
	Mean	**310.3**	**0.0508**	**1.9669**	**0.9197143**	**1.9647**	**11.9090**	**0.7149**	**3.0997**	**0.2067143**	**1.0447**
	SD	**30.02**	**0.00621**	**0.07835**	**0.09535**	**0.19099**	**1.92988**	**0.05621**	**0.10403**	**0.03112**	**0.06377**
12 mg/kg	05-005	326	0 055	2 087	0.978	2.086	12.866	0.762	3.245	0 200	1 150
	05-009	296	0 045	1.942	0.855	1.884	11.318	0.683	3.106	0 165	1 133
	05-019	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-021	337	0 046	2.096	1.048	2.253	13.893	0 703	2.877	0.204	0 997
	05-027	330	0.045	1 994	0.981	2.168	13.040	0.633	3.166	0.265	1.012
	05-031	313	0.042	2 097	0.889	1.930	12.306	0.695	3 049	0.230	0.963
	05-047	306	0.055	1.982	0.900	1 842	12.248	0.700	3.071	0.240	0.955
	05-048	348	0.044	2 091	0 957	2.080	13.626	0.716	3.119	0.243	1.033
	05-058	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-063	350	0.050	1.961	0 959	2.040	12.811	0.704	3.128	0 171	1.063
	Mean	**325.8**	**0.0478**	**2.0313**	**0.945875**	**2.0354**	**12.7635**	**0.6995**	**3.0951**	**0.2148**	**1.0383**
	SD	**19.51**	**0.00501**	**0.06751**	**0.06163**	**0.14189**	**0.81709**	**0.03571**	**0.10660**	**0.0356881**	**0.07279**
15 mg/kg	05-008	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-010	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-018	304	0.060	2.017	0.995	2.089	11.853	0.591	2.719	0 149	0.977
	05-022	323	0.048	2.033	0.930	2.114	12.338	0.723	3 094	0 200	0.990
	05-025	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-030	334	0.044	2 102	0.930	2.041	13.760	0.654	2 933	0 223	0.941
	05-032	315	0.045	1.973	0.912	1.774	11.508	0.678	2.929	0 143	0.978
	05-035	341	0 062	2.010	0.885	2.157	13.623	0.737	3.208	0.208	0.936
	05-043	334	0 072	2.081	1.018	2.131	12.337	0.755	2.801	0 150	1.225
	05-057	335	0.061	2 180	1.569	2.266	12.255	0.941	3.222	0 223	1.051
	Mean	**326.6**	**0.0560**	**2.0566**	**1.0341**	**2.0817**	**12.5249**	**0.7256**	**2.9866**	**0.1851**	**1.0140**
	SD	**13.20**	**0.01050**	**0.06973**	**0.24039**	**0.15248**	**0.85244**	**0.11023**	**0.19503**	**0.03635**	**0.10045**

No data
(f) = Animal died on study

Table R-8
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

90-Day Individual Organ Weights
Female Rats

ABSOLUTE ORGAN WEIGHTS (grams)

	Animal ID	Body Weight	Adrenals	Brain	Heart	Kidneys	Liver	Ovaries	Spleen	Thymus	Uterus
Methylcellulose Control	05-076	185	0.070	1.790	0.719	1.341	6.500	0.123	0.478	0.211	0.471
	05-077	179	0.064	1.689	0.566	1.310	6.589	0.076	0.410	0.145	0.465
	05-084	166	0.067	1.695	0.632	1.220	5.551	0.140	0.407	0.109	0.590
	05-088	172	0.072	1.719	0.590	1.183	5.612	0.108	0.433	0.249	0.510
	05-098	175	0.056	1.674	0.625	1.295	6.211	0.138	0.444	0.206	0.488
	05-100	177	0.067	1.773	0.665	1.189	6.073	0.120	0.441	0.208	1.077
	05-101	180	0.066	1.789	0.599	1.307	6.740	0.133	0.483	0.114	0.485
	05-114	166	0.065	1.880	0.536	1.105	4.722	0.116	0.428	0.232	0.295
	05-120	182	0.055	1.773	0.641	1.344	6.412	0.142	0.483	0.216	0.790
	05-127	184	0.056	1.711	0.646	1.302	6.804	0.127	0.460	0.244	0.500
	Mean	**176.6**	**0.0638**	**1.7493**	**0.6219**	**1.2596**	**6.1214**	**0.1223**	**0.4467**	**0.1934**	**0.5671**
	SD	**6.83**	**0.00607**	**0.06331**	**0.05206**	**0.08021**	**0.65393**	**0.01966**	**0.02846**	**0.05175**	**0.21722**
4 mg/kg	05-072	169	0.058	1.762	0.584	1.228	5.151	0.097	0.402	0.192	0.425
	05-078	177	0.069	1.729	0.657	1.226	6.748	0.112	0.428	0.178	0.328
	05-081	172	0.055	1.580	0.645	1.204	5.825	0.096	0.410	0.079	0.301
	05-090	174	0.078	1.674	0.564	1.291	6.433	0.135	0.491	0.199	0.650
	05-094	176	0.066	1.820	0.583	1.349	6.365	0.134	0.458	0.235	0.637
	05-095	174	0.071	1.664	0.592	1.180	6.126	0.115	0.479	0.219	1.282
	05-105	178	0.065	1.740	0.557	1.392	6.224	0.122	0.457	0.198	0.577
	05-115	180	0.068	1.813	0.606	1.352	6.187	0.125	0.471	0.222	0.480
	05-135	193	0.066	1.834	0.694	1.312	6.857	0.130	0.474	0.131	1.347
	05-136	168	0.065	1.568	0.607	1.222	5.659	0.104	0.422	0.136	0.506
	Mean	**176.1**	**0.0661**	**1.7184**	**0.6089**	**1.2756**	**6.1575**	**0.1170**	**0.4492**	**0.1789**	**0.6533**
	SD	**7.05**	**0.00640**	**0.09535**	**0.04366**	**0.07318**	**0.50939**	**0.01457**	**0.03130**	**0.04907**	**0.36763**
8 mg/kg	05-071	176	0.050	1.791	0.586	1.280	5.811	0.100	0.406	0.172	0.465
	05-074	169	0.058	1.836	0.562	1.218	5.541	0.116	0.413	0.208	0.515
	05-075	165	0.065	1.790	0.551	1.189	5.070	0.125	0.442	0.190	0.299
	05-085	210	0.069	2.052	0.643	1.282	7.050	0.099	0.470	0.225	0.305
	05-086	195	0.094	1.926	0.642	1.415	7.265	0.132	0.553	0.233	0.868
	05-092	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-102	180	0.047	1.770	0.623	1.323	6.231	0.144	0.483	0.258	0.920
	05-106	180	0.066	1.705	0.609	1.242	5.994	0.110	0.488	0.230	0.326
	05-108	221	0.061	1.957	0.630	1.486	7.506	0.130	0.486	0.237	0.582
	05-112	231	0.061	1.812	0.770	1.442	8.237	0.169	0.598	0.203	0.520
	Mean	**191.9**	**0.0634**	**1.8488**	**0.6240**	**1.3197**	**6.5228**	**0.1250**	**0.4821**	**0.2173**	**0.5333**
	SD	**23.71**	**0.01354**	**0.10849**	**0.06411**	**0.10498**	**1.04163**	**0.02230**	**0.06208**	**0.02646**	**0.22888**
10 mg/kg	05-073	216	0.057	1.843	0.680	1.443	8.137	0.128	0.540	0.235	0.808
	05-083	175	0.063	1.777	0.618	1.373	6.089	0.141	0.448	0.262	0.912
	05-091	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-109	191	0.079	1.703	0.650	1.360	6.979	0.133	0.556	0.236	0.451
	05-110	205	0.095	1.877	0.713	1.494	7.079	0.122	0.551	0.283	0.528
	05-111	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-117	207	0.069	1.805	0.679	1.417	7.060	0.118	0.559	0.093	0.301
	05-130	216	0.067	1.792	0.685	1.461	7.075	0.127	0.576	0.234	0.357
	05-131	191	0.064	1.767	0.634	1.338	6.312	0.136	0.539	0.223	0.507
	05-132	233	0.072	1.575	0.729	1.484	8.913	0.164	0.629	0.277	0.773
	Mean	**204.3**	**0.0708**	**1.7674**	**0.6735**	**1.4213**	**7.2055**	**0.1336**	**0.5498**	**0.2304**	**0.5796**
	SD	**18.20**	**0.01177**	**0.09335**	**0.03787**	**0.05893**	**0.92069**	**0.01433**	**0.05023**	**0.05968**	**0.22415**
12 mg/kg	05-080	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-082	218	0.063	1.888	0.735	1.352	7.750	0.171	0.546	0.292	0.538
	05-087	208	0.069	1.821	0.587	1.313	6.864	0.140	0.522	0.258	0.533
	05-096	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-121	224	0.083	1.820	0.722	1.567	7.879	0.138	0.505	0.246	0.303
	05-122	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-123	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-124	201	0.074	1.892	0.641	1.346	6.347	0.119	0.540	0.281	0.318
	05-128	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-134	193	0.039	1.673	0.652	1.371	6.410	0.138	0.507	0.201	0.272
	Mean	**208.8**	**0.0656**	**1.8188**	**0.6674**	**1.3898**	**7.0500**	**0.1412**	**0.5240**	**0.2556**	**0.3928**
	SD	**12.52**	**0.01658**	**0.08862**	**0.06113**	**0.10124**	**0.72726**	**0.01873**	**0.01867**	**0.03553**	**0.13133**
15 mg/kg	05-093	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-097	203		1.831	0.625	1.384	6.938	0.139	0.458	0.248	0.318
	05-099	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-104	215	0.067	1.832	0.467	1.378	7.719	0.138	0.564	0.246	0.484
	05-107	230	0.083	1.847	0.743	1.531	8.384	0.127	0.582	0.2	0.455
	05-113	261	0.066	1.934	0.801	1.547	9.829	0.151	0.696	0.336	0.652
	05-116	217	0.058	1.839	0.651	1.439	7.130	0.110	0.519	0.236	0.325
	05-126	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-129	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-133	204	0.069	1.862	0.654	1.412	6.946	0.110	0.501	0.114	0.531
	Mean	**221.7**	**0.0686**	**1.8575**	**0.6568**	**1.4485**	**7.8243**	**0.1292**	**0.5533**	**0.2300**	**0.4608**
	SD	**21.65**	**0.00907**	**0.03919**	**0.11428**	**0.07357**	**1.12979**	**0.01668**	**0.08282**	**0.07240**	**0.12719**

No data
(f) = Animal died on study

Table R-9
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

90-Day Individual Organ Weights
Male Rats

% Body Weight

	Animal ID	Adrenals	Brain	Heart	Kidneys	Liver	Spleen	Testes	Thymus	Epididymides
Methylcellulose	05-011	0.013	0.570	0.272	0.584	3.699	0.226	0.991	0.056	0.330
Control	05-012		0.580	0.310	0.665	3.818	0.211	1.004	0.079	0.376
	05-016	0.014	0.631	0.277	0.602	3.442	0.222	1.020	0.088	0.339
	05-020	0.014	0.646	0.276	0.630	3.550	0.221	1.011	0.024	0.341
	05-023	0.018	0.574	0.293	0.648	4.099	0.229	1.056	0.057	0.323
	05-052	0.014	0.671	0.325	0.594	3.463	0.233	1.130	0.093	0.364
	05-060	0.017	0.560	0.292	0.604	3.695	0.212	1.007	0.092	0.333
	05-064	0.016	0.626	0.291	0.594	3.809	0.206	1.028	0.084	0.333
	05-066	0.014	0.588	0.302	0.658	4.001	0.214	0.920	0.090	0.304
	05-070	0.013	0.611	0.290	0.635	3.880	0.201	0.973	0.086	0.368
	Mean	**0.0149**	**0.6056**	**0.2928**	**0.6215**	**3.7455**	**0.2173**	**1.0140**	**0.0749**	**0.3412**
	SD	**0.00162**	**0.03713**	**0.01633**	**0.02943**	**0.21911**	**0.01051**	**0.05454**	**0.02253**	**0.02199**
4 mg/kg	05-001	0.016	0.633	0.325	0.635	3.748	0.213	1.060	0.076	0.339
	05-007	0.015	0.583	0.284	0.630	4.020	0.204	0.986	0.095	0.390
	05-013	0.011	0.734	0.285	0.691	3.488	0.254	1.120	0.088	0.398
	05-028	0.021	0.641	0.301	0.622	3.852	0.230	1.053	0.050	0.390
	05-033	0.005	0.634	0.318	0.612	3.644	0.217	1.059	0.043	0.347
	05-039	0.018	0.623	0.302	0.639	3.714	0.228	1.025	0.101	0.374
	05-041	0.017	0.597	0.329	0.651	4.065	0.211	1.037	0.025	0.325
	05-055	0.020	0.612	0.292	0.618	3.876	0.223	1.007	0.097	0.329
	05-062	0.018	0.647	0.309	0.656	3.618	0.236	1.038	0.066	0.349
	05-067	0.017	0.688	0.304	0.655	3.475	0.226	1.137	0.100	0.363
	Mean	**0.0158**	**0.6394**	**0.3048**	**0.6409**	**3.7500**	**0.2243**	**1.0522**	**0.0740**	**0.3603**
	SD	**0.00456**	**0.04386**	**0.01570**	**0.02331**	**0.20334**	**0.01439**	**0.04645**	**0.02695**	**0.02643**
8 mg/kg	05-003	0.016	0.721	0.293	0.629	3.391	0.218	1.075	0.042	0.353
	05-006	0.018	0.655	0.279	0.633	3.559	0.242	1.087	0.087	0.329
	05-015	0.018	0.727	0.302	0.688	3.664	0.246	1.139	0.108	0.372
	05-034		0.631	0.263	0.664	3.740	0.207	0.991	0.040	0.302
	05-037	0.016	0.642	0.306	0.650	3.863	0.221	1.052	0.082	0.357
	05-045	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-046	0.016	0.626	0.301	0.644	3.813	0.210	0.964	0.086	0.336
	05-051	0.015	0.618	0.302	0.650	4.061	0.223	1.034	0.098	0.332
	05-068	0.016	0.653	0.317	0.671	3.756	0.242	1.067	0.077	0.352
	05-069	0.017	0.701	0.319	0.667	3.543	0.217	1.138	0.070	0.366
	Mean	**0.0166**	**0.6638**	**0.2980**	**0.6552**	**3.7100**	**0.2253**	**1.0608**	**0.0768**	**0.3442**
	SD	**0.00104**	**0.04192**	**0.01768**	**0.01898**	**0.19831**	**0.01468**	**0.05918**	**0.02315**	**0.02176**
10 mg/kg	05-017	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-024	0.018	0.746	0.314	0.631	3.123	0.274	1.222	0.092	0.376
	05-040		0.629	0.297	0.621	3.820	0.215	0.883	0.065	0.297
	05-042	0.016	0.565	0.277	0.643	3.856	0.187	0.882	0.061	0.312
	05-049	0.016	0.665	0.278	0.627	3.907	0.258	1.047	0.084	0.360
	05-050	0.015	0.619	0.287	0.640	3.738	0.240	1.044	0.051	0.340
	05-053	0.017	0.636	0.307	0.649	4.233	0.211	1.001	0.062	0.337
	05-054	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-056	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-065	0.018	0.607	0.318	0.621	4.050	0.240	0.978	0.058	0.347
	Mean	**0.0166**	**0.6382**	**0.2967**	**0.6332**	**3.8181**	**0.2324**	**1.0083**	**0.0675**	**0.3385**
	SD	**0.00118**	**0.05644**	**0.01674**	**0.01090**	**0.34748**	**0.02976**	**0.11632**	**0.01488**	**0.02687**
12 mg/kg	05-005	0.017	0.640	0.300	0.640	3.947	0.234	0.995	0.061	0.353
	05-009	0.015	0.656	0.289	0.636	3.824	0.231	1.049	0.056	0.383
	05-019	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-021	0.014	0.622	0.311	0.669	4.123	0.209	0.854	0.061	0.296
	05-027	0.014	0.604	0.297	0.657	3.952	0.192	0.959	0.080	0.307
	05-031	0.013	0.670	0.284	0.617	3.932	0.222	0.974	0.073	0.308
	05-047	0.018	0.648	0.294	0.602	4.003	0.229	1.004	0.078	0.312
	05-048	0.013	0.601	0.275	0.598	3.916	0.206	0.896	0.070	0.297
	05-058	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-063	0.014	0.560	0.274	0.583	3.660	0.201	0.894	0.049	0.304
	Mean	**0.0147**	**0.6252**	**0.2905**	**0.6251**	**3.9193**	**0.2153**	**0.9532**	**0.0661**	**0.3198**
	SD	**0.00185**	**0.03575**	**0.01268**	**0.03022**	**0.13440**	**0.01555**	**0.06624**	**0.01121**	**0.03115**
15 mg/kg	05-008	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-010	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-018	0.020	0.663	0.327	0.687	3.899	0.194	0.894	0.049	0.321
	05-022	0.015	0.629	0.288	0.654	3.820	0.224	0.958	0.062	0.307
	05-025	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-030	0.013	0.629	0.278	0.611	4.120	0.196	0.878	0.067	0.282
	05-032	0.014	0.626	0.290	0.563	3.653	0.215	0.930	0.045	0.310
	05-035	0.018	0.589	0.260	0.633	3.995	0.216	0.941	0.061	0.274
	05-043	0.022	0.623	0.305	0.638	3.694	0.226	0.839	0.045	0.367
	05-057	0.018	0.651	0.468	0.676	3.658	0.281	0.962	0.067	0.314
	Mean	**0.0171**	**0.6303**	**0.3166**	**0.6376**	**3.8341**	**0.2218**	**0.9145**	**0.0565**	**0.3107**
	SD	**0.00310**	**0.02330**	**0.07018**	**0.04187**	**0.18039**	**0.02891**	**0.04569**	**0.00975**	**0.03010**

No data
(f) = Animal Died on Study

Table R-10
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

90-Day Individual Organ Weights
Female Rats

% Body Weight

	Animal ID	Adrenals	Brain	Heart	Kidneys	Liver	Ovaries	Spleen	Thymus	Uterus
Methylcellulose Control	05-076	0.038	0.968	0.389	0.725	3.514	0.066	0.258	0.114	0.255
	05-077	0.036	0.944	0.316	0.732	3.681	0.042	0.229	0.081	0.260
	05-084	0.040	1.021	0.381	0.735	3.344	0.084	0.245	0.066	0.355
	05-088	0.042	0.999	0.343	0.688	3.263	0.063	0.252	0.145	0.297
	05-098	0.032	0.957	0.357	0.740	3.549	0.079	0.254	0.118	0.279
	05-100	0.038	1.002	0.376	0.672	3.431	0.068	0.249	0.118	0.608
	05-101	0.037	0.994	0.333	0.726	3.744	0.074	0.268	0.063	0.269
	05-114	0.039	1.133	0.323	0.666	2.845	0.070	0.258	0.140	0.178
	05-120	0.030	0.974	0.352	0.738	3.523	0.078	0.265	0.119	0.434
	05-127	0.030	0.930	0.351	0.708	3.698	0.069	0.250	0.133	0.272
	Mean	**0.0362**	**0.9920**	**0.3520**	**0.7129**	**3.4591**	**0.0694**	**0.2529**	**0.1095**	**0.3207**
	SD	**0.00409**	**0.05688**	**0.02435**	**0.02815**	**0.26521**	**0.01149**	**0.01106**	**0.02943**	**0.12145**
4 mg/kg	05-072	0.034	1.043	0.346	0.727	3.048	0.057	0.238	0.114	0.251
	05-078	0.039	0.977	0.371	0.693	3.812	0.063	0.242	0.101	0.185
	05-081	0.032	0.919	0.375	0.700	3.387	0.056	0.238	0.046	0.175
	05-090	0.045	0.962	0.324	0.742	3.697	0.078	0.282	0.114	0.374
	05-094	0.038	1.034	0.331	0.766	3.616	0.076	0.260	0.134	0.362
	05-095	0.041	0.956	0.340	0.678	3.521	0.066	0.275	0.126	0.737
	05-105	0.037	0.978	0.313	0.782	3.497	0.069	0.257	0.111	0.324
	05-115	0.038	1.007	0.337	0.751	3.437	0.069	0.262	0.123	0.267
	05-135	0.034	0.950	0.360	0.680	3.553	0.067	0.246	0.068	0.698
	05-136	0.039	0.933	0.361	0.727	3.368	0.062	0.251	0.081	0.301
	Mean	**0.0376**	**0.9759**	**0.3458**	**0.7246**	**3.4936**	**0.0664**	**0.2551**	**0.1017**	**0.3674**
	SD	**0.00366**	**0.04102**	**0.02056**	**0.03630**	**0.20852**	**0.00713**	**0.01517**	**0.02817**	**0.19601**
8 mg/kg	05-071	0.028	1.018	0.333	0.727	3.302	0.057	0.231	0.098	0.264
	05-074	0.034	1.086	0.333	0.721	3.279	0.069	0.244	0.123	0.305
	05-075	0.039	1.085	0.334	0.721	3.073	0.076	0.268	0.115	0.181
	05-085	0.033	0.977	0.306	0.610	3.357	0.047	0.224	0.107	0.145
	05-086	0.048	0.988	0.329	0.726	3.726	0.068	0.284	0.119	0.445
	05-092	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-102	0.026	0.983	0.346	0.735	3.462	0.080	0.268	0.143	0.511
	05-106	0.037	0.947	0.338	0.690	3.330	0.061	0.271	0.128	0.181
	05-108	0.028	0.886	0.285	0.672	3.396	0.059	0.220	0.107	0.263
	05-112	0.026	0.784	0.333	0.624	3.566	0.073	0.259	0.088	0.225
	Mean	**0.0333**	**0.9727**	**0.3264**	**0.6918**	**3.3878**	**0.0655**	**0.2521**	**0.1143**	**0.2801**
	SD	**0.00731**	**0.09459**	**0.01885**	**0.04676**	**0.18514**	**0.01040**	**0.02309**	**0.01659**	**0.12376**
10 mg/kg	05-073	0.026	0.853	0.315	0.668	3.767	0.059	0.250	0.109	0.374
	05-083	0.036	1.015	0.353	0.785	3.479	0.081	0.256	0.150	0.521
	05-091	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-109	0.041	0.892	0.340	0.712	3.654	0.070	0.291	0.124	0.236
	05-110	0.046	0.916	0.348	0.729	3.453	0.060	0.269	0.138	0.258
	05-111	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-117	0.033	0.872	0.328	0.685	3.411	0.057	0.270	0.045	0.145
	05-130	0.031	0.830	0.317	0.676	3.275	0.059	0.267	0.108	0.165
	05-131	0.034	0.925	0.332	0.701	3.305	0.071	0.282	0.117	0.265
	05-132	0.031	0.676	0.313	0.637	3.825	0.070	0.270	0.119	0.332
	Mean	**0.0349**	**0.8723**	**0.3308**	**0.6990**	**3.5212**	**0.0658**	**0.2693**	**0.1136**	**0.2871**
	SD	**0.00634**	**0.09729**	**0.01536**	**0.04459**	**0.20579**	**0.00838**	**0.01309**	**0.03118**	**0.12142**
12 mg/kg	05-080	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-082	0.029	0.866	0.337	0.620	3.555	0.078	0.250	0.134	0.247
	05-087	0.033	0.875	0.282	0.631	3.300	0.067	0.251	0.124	0.256
	05-096	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-121	0.037	0.813	0.322	0.700	3.517	0.062	0.225	0.110	0.135
	05-122	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-123	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-124	0.037	0.941	0.319	0.670	3.158	0.059	0.269	0.140	0.158
	05-128	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-134	0.020	0.867	0.338	0.710	3.321	0.072	0.263	0.104	0.141
	Mean	**0.0312**	**0.8724**	**0.3197**	**0.6662**	**3.3703**	**0.0676**	**0.2516**	**0.1224**	**0.1875**
	SD	**0.00700**	**0.04587**	**0.02262**	**0.04004**	**0.16456**	**0.00773**	**0.01658**	**0.01525**	**0.05915**
15 mg/kg	05-093	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-097		0.902	0.308	0.682	3.418	0.068	0.226	0.122	0.157
	05-099	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-104	0.031	0.852	0.217	0.641	3.590	0.064	0.262	0.114	0.225
	05-107	0.036	0.803	0.323	0.666	3.645	0.055	0.253	0.087	0.198
	05-113	0.025	0.741	0.307	0.593	3.766	0.058	0.267	0.129	0.250
	05-116	0.027	0.847	0.300	0.663	3.286	0.051	0.239	0.109	0.150
	05-126	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-129	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-133	0.034	0.913	0.321	0.692	3.405	0.054	0.246	0.056	0.260
	Mean	**0.0306**	**0.8431**	**0.2959**	**0.6561**	**3.5183**	**0.0584**	**0.2487**	**0.1028**	**0.2066**
	SD	**0.00458**	**0.06395**	**0.03955**	**0.03563**	**0.17869**	**0.00671**	**0.01524**	**0.02709**	**0.04668**

No data
(f) = Animal died on study

Table R-11
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

90-Day Individual Organ Weights
Male Rats

% Brain Weight

	Animal ID	Adrenals	Heart	Kidneys	Liver	Spleen	Testes	Thymus	Epididymides
Methylcellulose Control	05-011	2.365	47.661	102.468	648.586	39.537	173.728	9.769	57.943
	05-012		53.528	114.689	658.599	36.383	173.183	13.591	64.872
	05-016	2.258	43.904	95.384	545.760	35.173	161.766	13.949	53.738
	05-020	2.219	42.751	97.584	549.606	34.172	156.509	3.698	52.811
	05-023	3.060	51.148	113.005	714.481	40.000	184.153	9.891	56.339
	05-052	2.106	48.382	88.495	515.819	34.720	168.362	13.867	54.186
	05-060	3.050	52.113	108.026	660.300	37.828	179.882	16.479	59.444
	05-064	2.559	46.520	94.780	608.188	32.856	164.125	13.408	53.224
	05-066	2.338	51.387	112.072	680.914	36.378	156.607	15.389	51.822
	05-070	2.142	47.425	103.876	635.135	32.840	159.255	14.125	60.173
	Mean	**2.4552**	**48.4819**	**103.0378**	**621.7388**	**35.9887**	**167.7570**	**12.4167**	**56.4552**
	SD	**0.36521**	**3.55353**	**8.88590**	**65.17254**	**2.53149**	**9.73833**	**3.71900**	**4.13050**
4 mg/kg	05-001	2.474	51.316	100.316	591.842	33.684	167.368	11.947	53.474
	05-007	2.599	48.676	108.046	689.055	34.933	169.015	16.292	66.767
	05-013	1.543	38.797	94.146	475.253	34.646	152.528	12.028	54.231
	05-028	3.315	46.915	97.042	601.071	35.900	164.355	7.802	60.785
	05-033	0.842	50.168	96.521	574.635	34.175	167.059	6.790	54.770
	05-039	2.810	48.390	102.453	595.912	36.587	164.384	16.147	59.939
	05-041	2.807	55.032	109.004	680.350	35.381	173.517	4.184	54.449
	05-055	3.268	47.666	100.985	633.195	36.359	164.575	15.768	53.734
	05-062	2.758	47.793	101.304	558.877	36.510	160.381	10.231	53.912
	05-067	2.517	44.183	95.190	505.313	32.886	165.324	14.541	52.740
	Mean	**2.4932**	**47.8937**	**100.5007**	**590.5503**	**35.1060**	**164.8508**	**11.5730**	**56.4801**
	SD	**0.75906**	**4.29763**	**5.05913**	**67.93971**	**1.26915**	**5.54034**	**4.26137**	**4.54087**
8 mg/kg	05-003	2.247	40.603	87.233	470.082	30.247	149.096	5.753	48.877
	05-006	2.771	42.603	96.602	543.283	37.010	165.917	13.330	50.183
	05-015	2.464	41.512	94.578	503.614	33.790	156.517	14.896	51.150
	05-034		41.679	105.185	592.840	32.741	157.037	6.420	47.802
	05-037	2.571	47.744	101.312	601.994	34.470	163.956	12.854	55.561
	05-045	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-046	2.498	48.152	102.997	609.491	33.616	154.146	13.786	53.746
	05-051	2.481	48.837	105.168	656.848	36.124	167.235	15.814	53.747
	05-068	2.430	48.494	102.853	575.383	37.137	163.444	11.833	53.988
	05-069	2.428	45.473	95.094	505.412	30.956	162.367	9.914	52.150
	Mean	**2.4860**	**45.0108**	**99.0024**	**562.1051**	**34.0100**	**159.9684**	**11.6223**	**51.9116**
	SD	**0.14765**	**3.40772**	**6.03623**	**60.61275**	**2.46886**	**6.06786**	**3.56853**	**2.60019**
10 mg/kg	05-017	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-024	2.400	42.045	84.611	418.727	36.776	163.850	12.363	50.391
	05-040		47.137	98.712	606.870	34.160	140.267	10.305	47.233
	05-042	2.891	49.045	113.836	682.860	33.196	156.221	10.738	55.292
	05-049	2.354	41.812	94.319	587.871	38.843	157.574	12.641	54.197
	05-050	2.423	46.311	103.393	603.823	38.826	168.713	8.293	54.981
	05-053	2.636	48.302	101.977	665.129	33.198	157.324	9.731	52.914
	05-054	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-056	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-065	2.950	52.311	102.360	666.962	39.577	161.013	9.489	57.129
	Mean	**2.6089**	**46.7090**	**99.8868**	**604.6061**	**36.3681**	**157.8517**	**10.5086**	**53.1624**
	SD	**0.26067**	**3.77389**	**8.97279**	**89.91823**	**2.81723**	**8.90849**	**1.56165**	**3.35520**
12 mg/kg	05-005	2.635	46.862	99.952	616.483	36.512	155.486	9.583	55.103
	05-009	2.317	44.027	97.013	582.801	35.170	159.938	8.496	58.342
	05-019	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-021	2.195	50.000	107.490	662.834	33.540	137.261	9.733	47.567
	05-027	2.257	49.198	108.726	653.962	31.745	158.776	13.290	50.752
	05-031	2.003	42.394	92.036	586.838	33.143	145.398	10.968	45.923
	05-047	2.775	45.409	92.936	617.962	35.318	154.945	12.109	48.184
	05-048	2.104	45.768	99.474	651.650	34.242	149.163	11.621	49.402
	05-058	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-063	2.550	48.904	104.029	653.289	35.900	159.510	8.720	54.207
	Mean	**2.3545**	**46.5700**	**100.2072**	**628.2274**	**34.4462**	**152.5598**	**10.5651**	**51.1850**
	SD	**0.27165**	**2.67529**	**6.21810**	**31.75012**	**1.58209**	**8.04021**	**1.70823**	**4.29055**
15 mg/kg	05-008	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-010	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-018	2.975	49.331	103.570	587.655	29.301	134.804	7.387	48.438
	05-022	2.361	45.745	103.984	606.886	35.563	152.189	9.838	48.697
	05-025	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-030	2.093	44.244	97.098	654.615	31.113	139.534	10.609	44.767
	05-032	2.281	46.224	89.914	583.274	34.364	148.454	7.248	49.569
	05-035	3.085	44.030	107.313	677.761	36.667	159.602	10.348	46.567
	05-043	3.460	48.919	102.403	592.840	36.281	134.599	7.208	58.866
	05-057	2.798	71.972	103.945	562.156	43.165	147.798	10.229	48.211
	Mean	**2.7218**	**50.0664**	**101.1753**	**609.3125**	**35.2077**	**145.2828**	**8.9811**	**49.3021**
	SD	**0.49428**	**9.87856**	**5.82984**	**41.60433**	**4.45521**	**9.36411**	**1.60723**	**4.50721**

No data
(f) = Animal died on study

Table R-12
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

90-Day Individual Organ Weights
Female Rats

% Brain Weight

	Animal ID	Adrenals	Heart	Kidneys	Liver	Ovaries	Spleen	Thymus	Uterus
Methylcellulose Control	05-076	3.911	40.168	74.916	363.128	6.872	26.704	11.788	26.313
	05-077	3.789	33.511	77.561	390.112	4.500	24.275	8.585	27.531
	05-084	3.953	37.286	71.976	327.493	8.260	24.012	6.431	34.808
	05-088	4.188	34.322	68.819	326.469	6.283	25.189	14.485	29.668
	05-098	3.345	37.336	77.360	371.027	8.244	26.523	12.306	29.152
	05-100	3.779	37.507	67.061	342.527	6.768	24.873	11.732	60.745
	05-101	3.689	33.482	73.058	376.747	7.434	26.998	6.372	27.110
	05-114	3.457	28.511	58.777	251.170	6.170	22.766	12.340	15.691
	05-120	3.102	36.153	75.804	361.647	8.009	27.242	12.183	44.557
	05-127	3.273	37.756	76.096	397.662	7.423	26.885	14.261	29.223
	Mean	**3.6487**	**35.6032**	**72.1427**	**350.7983**	**6.9962**	**25.5467**	**11.0482**	**32.4798**
	SD	**0.34309**	**3.26682**	**5.86587**	**42.45697**	**1.15678**	**1.54030**	**2.92382**	**12.26092**
4 mg/kg	05-072	3.292	33.144	69.694	292.338	5.505	22.815	10.897	24.120
	05-078	3.991	37.999	70.908	390.283	6.478	24.754	10.295	18.971
	05-081	3.481	40.823	76.203	368.671	6.076	25.949	5.000	19.051
	05-090	4.659	33.692	77.121	384.289	8.065	29.331	11.888	38.829
	05-094	3.626	32.033	74.121	349.725	7.363	25.165	12.912	35.000
	05-095	4.267	35.577	70.913	368.149	6.911	28.786	13.161	77.043
	05-105	3.736	32.011	80.000	357.701	7.011	26.264	11.379	33.161
	05-115	3.751	33.425	74.573	341.258	6.895	25.979	12.245	26.475
	05-135	3.599	37.841	71.538	373.882	7.088	25.845	7.143	73.446
	05-136	4.145	38.712	77.934	360.906	6.633	26.913	8.673	32.270
	Mean	**3.8547**	**35.5257**	**74.3003**	**358.7203**	**6.8024**	**26.1802**	**10.3593**	**37.8367**
	SD	**0.41094**	**3.12133**	**3.48329**	**27.62053**	**0.69901**	**1.88141**	**2.65625**	**20.79830**
8 mg/kg	05-071	2.792	32.719	71.468	324.456	5.583	22.669	9.604	25.963
	05-074	3.159	30.610	66.340	301.797	6.318	22.495	11.329	28.050
	05-075	3.631	30.782	66.425	283.240	6.983	24.693	10.615	16.704
	05-085	3.363	31.335	62.476	343.567	4.825	22.904	10.965	14.864
	05-086	4.881	33.333	73.468	377.207	6.854	28.712	12.098	45.067
	05-092	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-102	2.655	35.198	74.746	352.034	8.136	27.288	14.576	51.977
	05-106	3.871	35.718	72.845	351.554	6.452	28.622	13.490	19.120
	05-108	3.117	32.192	75.933	383.546	6.643	24.834	12.110	29.739
	05-112	3.366	42.494	79.581	454.581	9.327	33.002	11.203	28.698
	Mean	**3.4261**	**33.8203**	**71.4756**	**352.4425**	**6.7911**	**26.1354**	**11.7766**	**28.9092**
	SD	**0.66393**	**3.71743**	**5.41966**	**50.28639**	**1.32119**	**3.54948**	**1.51030**	**12.47726**
10 mg/kg	05-073	3.093	36.896	78.296	441.508	6.945	29.300	12.751	43.842
	05-083	3.545	34.778	77.265	342.656	7.935	25.211	14.744	51.322
	05-091	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-109	4.639	38.168	79.859	409.806	7.810	32.648	13.858	26.483
	05-110	5.061	37.986	79.595	377.144	6.500	29.355	15.077	28.130
	05-111	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-117	3.823	37.618	78.504	391.136	6.537	30.970	5.152	16.676
	05-130	3.739	38.225	81.529	394.810	7.087	32.143	13.058	19.922
	05-131	3.622	35.880	75.722	357.216	7.697	30.504	12.620	28.693
	05-132	4.571	46.286	94.222	565.905	10.413	39.937	17.587	49.079
	Mean	**4.0116**	**38.2296**	**80.6241**	**410.0227**	**7.6154**	**31.2584**	**13.1060**	**33.0183**
	SD	**0.66893**	**3.47546**	**5.76446**	**69.98630**	**1.25961**	**4.18678**	**3.60240**	**13.27755**
12 mg/kg	05-080	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-082	3.337	38.930	71.610	410.487	9.057	28.919	15.466	28.496
	05-087	3.789	32.235	72.103	376.936	7.688	28.666	14.168	29.270
	05-096	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-121	4.560	39.670	86.099	432.912	7.582	27.747	13.516	16.648
	05-122	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-123	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-124	3.911	33.879	71.142	335.465	6.290	28.541	14.852	16.808
	05-128	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-134	2.331	38.972	81.949	383.144	8.249	30.305	12.014	16.258
	Mean	**3.5858**	**36.7374**	**76.5805**	**387.7889**	**7.7732**	**28.8357**	**14.0034**	**21.4959**
	SD	**0.82663**	**3.42206**	**6.95966**	**36.83905**	**1.01480**	**0.93083**	**1.33043**	**6.75169**
15 mg/kg	05-093	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-097		34.134	75.587	378.919	7.591	25.014	13.545	17.368
	05-099	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-104	3.657	25.491	75.218	421.343	7.533	30.786	13.428	26.419
	05-107	4.494	40.227	82.891	453.925	6.876	31.511	10.828	24.635
	05-113	3.413	41.417	79.990	508.221	7.808	35.988	17.373	33.713
	05-116	3.154	35.400	78.249	387.711	5.982	28.222	12.833	17.673
	05-126	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-129	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-133	3.706	35.124	75.832	373.040	5.908	26.907	6.122	28.518
	Mean	**3.6846**	**35.2988**	**77.9613**	**420.5264**	**6.9495**	**29.7377**	**12.3549**	**24.7207**
	SD	**0.50289**	**5.64455**	**3.03952**	**52.66803**	**0.83865**	**3.89700**	**3.71897**	**6.35462**

No data
(f) = Animal died on study

APPENDIX S

SUMMARY OF 90-DAY CLINICAL CHEMISTRY AND INDIVIDUAL CLINICAL CHEMISTRY DATA

Table S-1
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Summary of Clinical Chemistry
Male Rats

Period		Methylcellulose Control	RDX in 1% Methylcellulose / 0.2% Tween 80				
			4 mg/kg	8 mg/kg	10 mg/kg	12 mg/kg	15 mg/kg
ALK P	Mean	172.70	172.00	170.00	196.14	207.88	190.71
(U/L)	S.D.	36.600	24.486	35.143	33.938	37.749	33.084
	N	10	10	9	7	8	7
ALT	Mean	64.80	100.50	141.00	49.57	56.13	52.71
(U/L)	S.D.	26.989	118.870	160.472	11.660	28.317	10.177
	N	10	10	9	7	8	7
AST	Mean	187.80	219.40	360.89	109.71	210.75	140.00
(U/L)	S.D.	171.459	300.704	441.791	29.539	336.298	123.177
	N	10	10	9	7	8	7
BUN	Mean	23.63	24.44	25.46	24.10	23.71	25.97
(mg/dL)	S.D.	2.052	1.877	1.702	1.204	1.681	2.065
	N	10	10	9	7	8	7
Ca	Mean	10.380	10.393	10.243	10.719	10.461	10.499
(mg/dL)	S.D.	0.2607	0.3113	0.3065	0.4981	0.2713	0.2219
	N	10	10	9	7	8	7
CHOL	Mean	77.59	75.37	69.96*	64.93*	63.65*	69.29*
(mg/dL)	S.D.	4.772	8.023	6.162	5.359	7.231	5.071
	N	10	10	9	7	8	7
CK	Mean	1691.80	1746.40	2094.22	1029.14	1738.88	1169.00
(U/L)	S.D.	1952.655	2834.214	2324.450	412.281	2580.521	1269.979
	N	10	10	9	7	8	7
CREA	Mean	0.411	0.391	0.378	0.410	0.401	0.431
(mg/dL)	S.D.	0.0351	0.0420	0.0217	0.0383	0.0557	0.0456
	N	10	10	9	7	8	7
GLU	Mean	216.25	206.87	199.59	220.06	196.84	192.11
(mg/dL)	S.D.	25.231	18.727	21.813	45.447	21.826	8.884
	N	10	10	9	7	8	7
LDH	Mean	2616.70	3178.10	4893.67	1348.86	2601.38	1730.14
(U/L)	S.D.	2211.743	4371.147	6258.513	521.327	4249.531	1573.624
	N	10	10	9	7	8	7
TBIL	Mean	0.173	0.170	0.207	0.100	0.244	0.111
(mg/dL)	S.D.	0.1505	0.1536	0.2200	0.00000	0.3716	0.0302
	N	10	10	9	7	8	7
TP	Mean	6.064	6.049	6.089	5.873	6.060	6.031
(g/dL)	S.D.	0.1244	0.2188	0.2381	0.2037	0.2237	0.1971
	N	10	10	9	7	8	7
TRIG	Mean	174.78	177.43	176.38	163.36	171.40	142.03
(mg/dL)	S.D.	27.454	51.060	61.973	26.127	26.263	35.060
	N	10	10	9	7	8	7
Na	Mean	146.69	146.75	146.44	147.03	146.16	146.6
(mmol/L)	S.D.	1.333	1.416	1.286	1.423	1.546	1.241
	N	10	10	9	7	8	7
K	Mean	5.046	5.402	5.537	5.344	5.585	5.500
(mmol/L)	S.D.	0.599	0.4439	0.6724	0.4591	0.7866	0.4771
	N	10	10	9	7	8	7
Cl	Mean	103.69	104.57	103.68	104.56	104.13	103.93
(mmol/L)	S.D.	0.865	0.872	0.821	1.388	0.255	1.089
	N	10	10	9	7	8	7

* p less than or equal to 0.05
ANOVA with Holm-Sidak Method

Table S-2
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Summary of Clinical Chemistry
Female Rats

Period		*Methylcellulose* Control	*RDX in 1% Methylcellulose / 0.2% Tween 80* 4 mg/kg	8 mg/kg	10 mg/kg	12 mg/kg	15 mg/kg
ALK P	Mean	149.70	163.20	167.22	178.50	162.40	164.00
(U/L)	S.D.	22.657	25.192	38.395	38.932	27.254	34.716
	N	10	10	9	8	5	6
ALT	Mean	72.20	56.20	50.33	147.25	76.60	55.83
(U/L)	S.D.	26.657	19.555	10.416	168.940	57.474	14.811
	N	10	10	9	8	5	6
AST	Mean	223.10	184.90	163.67	394.38	205.80	246.50
(U/L)	S.D.	131.703	118.134	86.825	288.016	96.482	196.797
	N	10	10	9	8	5	6
BUN	Mean	23.97	23.56	24.07	23.56	22.22	24.42
(mg/dL)	S.D.	1.538	2.674	1.679	2.396	2.605	2.369
	N	10	10	9	8	5	6
Ca	Mean	10.315	10.269	10.410	10.694	10.644	10.852
(mg/dL)	S.D.	0.4467	0.5311	0.4895	0.6927	0.6961	0.4549
	N	10	10	9	8	5	6
CHOL	Mean	83.13	82.54	76.43	79.54	79.84	81.97
(mg/dL)	S.D.	7.032	8.348	10.171	5.865	10.064	6.121
	N	10	10	9	8	5	6
CK	Mean	2708.60	1822.50	1986.00	3640.00	2546.40	3902.33
(U/L)	S.D.	1615.544	1499.095	1354.386	3145.126	1494.893	3104.271
	N	10	10	9	8	5	6
CREA	Mean	0.401	0.385	0.404	0.371	0.400	0.378
(mg/dL)	S.D.	0.0451	0.0462	0.0508	0.0336	0.0675	0.0504
	N	10	10	9	8	5	6
GLU	Mean	209.88	194.16	194.86	211.64	203.14	208.30
(mg/dL)	S.D.	20.305	21.353	26.455	37.928	37.238	24.061
	N	10	10	9	8	5	6
LDH	Mean	2927.00	2429.80	2140.67	5607.63	2880.40	3437.83
(U/L)	S.D.	1617.838	1457.161	1068.322	4077.827	1816.500	2741.071
	N	10	10	9	8	5	6
TBIL	Mean	0.277	0.284	0.229	0.323	0.296	0.407
(mg/dL)	S.D.	0.1609	0.2423	0.1115	0.1422	0.1812	0.2035
	N	10	10	9	8	5	6
TP	Mean	5.926	5.861	5.938	6.040	6.000	6.318
(g/dL)	S.D.	0.3472	0.3091	0.3002	0.1795	0.3899	0.2013
	N	10	10	9	8	5	6
TRIG	Mean	92.61	78.04	73.29	98.95	58.00	108.82
(mg/dL)	S.D.	36.179	25.538	20.063	20.418	23.543	28.281
	N	10	10	9	8	5	6
Na	Mean	145.97	146.81	146.71	145.28	144.90	146.76
(mmol/L)	S.D.	1.990	2.815	2.276	1.729	2.760	2.196
	N	9	9	9	8	5	6
K	Mean	5.272	5.387	5.277	6.289	5.902	5.716
(mmol/L)	S.D.	0.5692	0.5855	0.5516	1.0385	0.9038	0.9286
	N	9	9	9	8	5	6
Cl	Mean	105.97	105.72	105.80	104.90	104.70	104.86
(mmol/L)	S.D.	0.559	1.424	1.623	0.961	0.894	0.966
	N	9	9	9	8	5	6

Table B-3
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

90-Day Individual Clinical Chemistry
Male Rats

Dose	Animal ID	ALKP (U/L)	ALT (U/L)	AST (U/L)	BUN (mg/dL)	Ca (mg/dL)	CHOL (mg/dL)	CK (U/L)	CREA (mg/dL)	GLU (mg/dL)	LDH (U/L)	TBIL (mg/dL)	TP (g/dL)	TRIG (mg/dL)	Na (mmol/L)	K (mmol/L)	Cl (mmol/L)	Comments
Methylcellulose Control	05-011	139.0	136.0	604.0	26.4	10.00	74.3	6838.0	0.35	216.8	8078.0	0.58	6.24	168.4	145.0	6.06	105.0	1:3 dilution for CK and LDH
	05-012	197.0	46.0	82.0	23.2	10.64	68.4	483.0	0.40	217.1	1275.0	0.10	6.09	179.4	147.1	4.45	102.9	
	05-016	133.0	67.0	255.0	23.8	10.26	72.4	1869.0	0.37	204.6	4004.0	0.22	5.98	193.6	145.3	4.90	105.2	1:3 dilution for LDH
	05-020	244.0	57.0	82.0	23.7	9.89	80.9	348.0	0.40	172.8	1200.0	0.11	6.19	160.8	148.4	5.85	103.6	
	05-023	145.0	55.0	154.0	26.8	10.55	78.5	1521.0	0.43	269.9	1943.0	0.11	6.00	213.4	146.4	4.71	103.2	
	05-052	202.0	37.0	73.0	25.0	10.54	82.1	1322.0	0.42	199.0	1274.0	0.10	6.04	190.2	148.1	5.52	104.1	
	05-060	133.0	69.0	338.0	22.9	10.40	76.6	2613.0	0.40	216.4	3982.0	0.21	5.82	184.5	144.6	4.74	103.5	1:3 dilution for CK and LDH
	05-064	186.0	58.0	87.0	21.5	10.51	79.7	437.0	0.42	223.0	1002.0	0.10	6.02	144.1	146.8	4.19	102.5	
	05-066	162.0	69.0	137.0	22.9	10.65	78.8	1014.0	0.46	236.1	1900.0	0.10	6.06	119.6	147.6	5.10	103.7	
	05-070	186.0	54.0	66.0	20.1	10.36	84.2	471.0	0.46	206.8	1509.0	0.10	6.20	193.8	147.6	4.94	103.2	
	Mean	172.70	64.80	187.80	23.63	10.380	77.59	1691.30	0.411	216.25	2616.70	0.173	6.064	174.78	146.69	5.046	103.69	
	SD	36.600	26.989	171.459	2.052	0.2607	4.772	1952.655	0.0351	25.231	2211.743	0.1505	0.1244	27.454	1.333	0.5998	0.865	
4 mg/kg	05-001	185.0	55.0	109.0	22.9	10.14	74.3	905.0	0.36	197.0	1101.0	0.10	6.22	108.3	145.6	5.29	104.3	
	05-007	199.0	60.0	80.0	23.8	10.45	77.3	576.0	0.38	190.5	1370.0	0.10	6.07	156.2	145.0	5.33	104.9	
	05-013	134.0	429.0	1047.0	27.7	9.70	62.9	9745.0	0.35	226.5	15005.0	0.36	5.91	92.9	147.7	5.81	105.4	1:3 dilution for AST and 1:6 dilution for CK and LDH
	05-028	206.0	46.0	83.0	25.6	10.25	81.9	689.0	0.47	175.3	1522.0	0.10	6.11	218.5	148.7	5.60	105.0	
	05-033	134.0	84.0	276.0	26.5	10.84	71.9	1626.0	0.35	216.4	4681.0	0.54	6.27	249.3	146.8	6.19	106.0	1:3 dilution for LDH
	05-039	190.0	40.0	73.0	24.2	10.58	70.1	565.0	0.42	203.8	856.0	0.10	5.97	209.5	146.8	4.90	103.7	
	05-041	173.0	55.0	106.0	23.5	10.52	87.9	617.0	0.34	203.0	1194.0	0.10	6.17	195.2	145.4	4.81	104.3	
	05-055	170.0	54.0	62.0	25.6	10.60	86.1	427.0	0.42	216.1	658.0	0.10	6.34	217.9	149.2	5.60	103.5	
	05-062	162.0	137.0	260.0	23.1	10.49	67.5	1163.0	0.40	240.8	3993.0	0.10	5.70	142.6	145.7	4.90	105.2	1:3 dilution for LDH
	05-067	167.0	45.0	98.0	21.5	10.36	73.8	1151.0	0.42	199.3	1401.0	0.10	5.73	183.9	146.6	5.59	103.4	
	Mean	172.00	108.50	219.30	24.44	10.393	75.37	1746.40	0.391	206.87	3178.10	0.170	6.049	177.43	146.75	5.402	104.57	
	SD	24.486	118.870	308.704	1.877	0.3113	8.923	2834.214	0.0429	18.727	4371.147	0.1536	0.2188	51.060	1.416	0.4439	0.872	
8 mg/kg	05-003	138.0	312.0	845.0	26.2	9.75	65.1	4335.0	0.35	189.5	11031.0	0.74	6.50	170.2	148.3	6.74	104.0	1:3 dilution for CK and 1:6 dilution for LDH
	05-006	190.0	39.0	95.0	23.1	10.11	61.7	789.0	0.37	179.3	1388.0	0.10	5.97	121.0	145.0	4.94	102.7	
	05-015	120.0	494.0	1324.0	26.7	9.82	73.7	7333.0	0.36	203.4	18832.0	0.38	6.26	187.4	144.4	6.47	103.3	1:3 dilution for AST and CK and 1:8 dilution for LDH
	05-034	213.0	45.0	73.0	22.9	10.66	61.7	414.0	0.39	179.3	476.0	0.10	6.06	169.9	146.7	5.39	103.3	
	05-037	174.0	61.0	159.0	27.2	10.21	70.5	983.0	0.39	186.2	1656.0	0.14	6.22	192.8	145.7	5.71	103.7	
	05-045	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	
	05-046	177.0	49.0	148.0	25.4	10.39	77.2	1390.0	0.39	232.8	1826.0	0.10	5.98	210.0	147.3	4.72	103.8	
	05-051	223.0	71.0	92.0	27.5	10.50	78.4	547.0	0.37	179.5	1726.0	0.10	6.23	308.5	147.8	5.22	103.1	
	05-068	137.0	167.0	437.0	25.9	10.46	69.1	2385.0	0.36	217.2	6390.0	0.10	5.87	94.2	146.0	5.44	105.6	1:3 dilution for CK and LDH
	05-069	158.0	31.0	75.0	24.2	10.29	72.2	672.0	0.42	229.1	918.0	0.10	5.71	133.4	146.8	5.20	103.6	
	Mean	170.00	141.00	368.89	25.46	10.243	69.94	3094.22	0.378	199.59	4893.67	0.207	6.089	176.38	146.44	5.537	103.68	
	SD	35.143	160.472	441.791	1.702	0.3665	6.162	2334.450	0.0217	21.813	6258.513	0.2280	0.2381	61.973	1.286	0.6724	0.821	
10 mg/kg	05-017	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	
	05-024	130.0	42.0	97.0	26.4	10.19	75.3	1186.0	0.45	192.8	1506.0	0.10	5.72	125.8	148.3	5.00	106.0	
	05-040	213.0	68.0	153.0	24.6	10.73	65.4	1354.0	0.38	237.8	2328.0	0.10	5.80	167.6	147.9	4.96	103.8	
	05-042	203.0	61.0	86.0	24.0	10.37	66.3	455.0	0.44	184.0	767.0	0.10	6.17	167.3	147.6	5.74	103.3	
	05-049	172.0	39.0	143.0	23.0	11.75	58.8	1617.0	0.43	313.6	1483.0	0.10	5.79	137.9	147.7	5.76	104.2	
	05-050	212.0	37.0	82.0	23.0	10.60	65.6	603.0	0.37	186.2	1037.0	0.10	5.99	195.0	147.2	5.64	105.4	
	05-053	228.0	53.0	122.0	24.4	10.76	60.6	1118.0	0.36	217.4	1408.0	0.10	5.59	155.8	144.1	4.65	106.4	
	05-054	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	
	05-056	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	
	05-065	215.0	47.0	85.0	23.3	10.63	62.5	871.0	0.44	208.6	913.0	0.10	6.05	194.1	146.4	5.66	102.8	
	Mean	196.14	49.57	109.71	24.10	10.719	64.93	1029.14	0.410	226.86	1348.86	0.100	5.873	163.36	147.03	5.344	104.56	
	SD	33.938	11.660	29.539	1.304	0.4981	5.359	412.281	0.0383	45.447	521.327	0.0000	0.2037	26.127	1.423	0.4591	1.388	
12 mg/kg	05-005	214.0	44.0	142.0	22.7	10.22	60.6	1114.0	0.36	177.5	1614.0	0.10	6.11	143.2	144.9	5.44	104.2	
	05-009	249.0	47.0	83.0	22.8	10.51	56.8	905.0	0.46	235.7	944.0	0.10	5.85	150.7	147.7	4.62	103.8	
	05-019	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	
	05-021	211.0	41.0	110.0	22.5	10.48	71.5	812.0	0.41	175.5	906.0	0.19	6.15	202.6	146.5	6.21	104.2	
	05-027	132.0	125.0	1041.0	26.5	10.25	51.2	8074.0	0.29	209.5	13101.0	1.16	6.41	156.0	143.0	7.12	104.4	1:3 dilution for AST and CK and 1:6 dilution for LDH
	05-031	248.0	48.0	82.0	25.0	10.20	66.4	1417.0	0.39	216.2	1018.0	0.10	5.79	144.2	146.2	4.96	103.8	
	05-047	225.0	47.0	83.0	25.0	11.04	67.6	515.0	0.41	191.3	1273.0	0.10	5.80	175.1	146.6	5.20	104.3	
	05-048	186.0	57.0	77.0	23.8	10.45	72.0	388.0	0.44	176.6	864.0	0.10	6.21	204.1	146.8	5.78	104.4	
	05-058	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	
	05-063	198.0	40.0	68.0	21.4	10.54	63.1	686.0	0.45	192.4	1091.0	0.10	6.16	195.3	147.6	5.35	103.9	
	Mean	207.88	56.13	218.75	23.71	10.461	63.65	1738.88	0.401	196.84	3601.38	0.344	6.068	171.60	146.16	5.585	104.13	
	SD	37.749	28.317	336.298	1.681	0.2713	7.231	2580.521	0.0557	21.826	4249.531	0.3716	0.2237	26.363	1.546	0.7866	0.255	
15 mg/kg	05-008	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	
	05-010	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	
	05-018	195.0	49.0	79.0	24.1	10.80	73.8	265.0	0.38	199.4	738.0	0.10	6.15	155.9	146.6	5.91	104.5	
	05-022	170.0	49.0	100.0	24.1	10.38	72.6	975.0	0.39	190.0	1930.0	0.18	6.16	159.8	146.3	4.98	101.9	
	05-025	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	
	05-030	234.0	46.0	78.0	25.7	10.46	75.7	447.0	0.44	180.9	801.0	0.10	6.15	204.5	148.1	5.85	104.6	
	05-032	201.0	43.0	91.0	26.5	10.83	69.5	1143.0	0.46	189.7	983.0	0.10	6.19	121.8	148.2	5.68	103.2	
	05-035	227.0	72.0	109.0	25.8	10.32	66.4	805.0	0.46	207.3	1038.0	0.10	5.94	129.6	146.3	5.12	104.2	
	05-043	162.0	61.0	418.0	25.4	10.31	61.7	3966.0	0.39	192.7	5173.0	0.10	5.64	95.3	144.6	4.92	103.9	1:3 dilution for CK and LDH
	05-057	146.0	49.0	105.0	30.2	10.39	65.3	582.0	0.50	184.8	1448.0	0.10	5.99	127.3	146.1	6.04	105.2	
	Mean	190.71	52.71	148.00	25.97	10.499	69.29	1169.00	0.431	192.11	1730.14	0.111	6.031	142.03	146.68	5.500	103.93	
	SD	33.084	10.177	123.177	2.065	0.2219	5.071	1269.979	0.0456	8.884	1573.624	0.0302	0.1971	35.060	1.241	0.4771	1.089	

(1) = Animal died on study

Table B-4
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

90-Day Individual Clinical Chemistry
Female Rats

Dose	Animal ID	ALKP (U/L)	ALT (U/L)	AST (U/L)	BUN (mg/dL)	Ca (mg/dL)	CHOL (mg/dL)	CK (U/L)	CREA (mg/dL)	GLU (mg/dL)	LDH (U/L)	TBIL (mg/dL)	TP (g/dL)	TRIG (mg/dL)	Na (mmol/L)	K (mmol/L)	Cl (mmol/L)	Comments
Methylcellulose Control	05-076	113.0	101.0	553.0	26.1	10.20	83.9	4250.0	0.37	240.3	5866.0	0.67	6.29	92.2	147.4	6.06	106.5	hemolyzed sample; CK and LDH diluted 1:3
	05-077	150.0	96.0	276.0	23.4	10.65	81.3	5347.0	0.39	224.6	4627.0	0.11	6.10	77.7				short sample; slightly hemolyzed; CK and LDH diluted 1:3
	05-084	177.0	52.0	165.0	22.6	9.75	76.6	1750.0	0.37	204.2	1678.0	0.23	5.51	105.3	145.3	5.16	106.2	
	05-088	130.0	58.0	119.0	25.0	9.85	87.0	1326.0	0.42	195.3	1266.0	0.23	5.85	70.4	145.2	4.77	106.3	
	05-098	130.0	46.0	156.0	22.4	10.03	81.8	3107.0	0.31	187.5	4222.0	0.40	5.87	96.1	143.5	5.05	106.3	CK and LDH diluted 1:3
	05-100	154.0	52.0	143.0	24.8	10.37	82.2	1400.0	0.45	233.1	1347.0	0.28	5.76	99.1	147.8	5.20	106.5	
	05-101	157.0	80.0	201.0	25.9	10.21	81.5	4522.0	0.44	214.9	3406.0	0.25	5.86	75.0	147.4	5.95	105.5	hemolyzed sample; CK and LDH diluted 1:3
	05-114	171.0	43.0	116.0	24.1	10.10	70.2	794.0	0.39	187.8	1534.0	0.17	5.35	23.9	142.9	4.39	105.9	
	05-120	181.0	121.0	197.0	21.4	11.18	93.4	1257.0	0.46	186.4	1879.0	0.14	6.19	161.9	148.7	5.86	105.7	
	05-127	134.0	73.0	305.0	24.0	10.81	93.4	3333.0	0.41	224.7	3445.0	0.29	6.48	124.5	145.5	5.01	104.8	CK and LDH diluted 1:3
	Mean	149.70	72.20	223.10	23.97	10.315	82.13	2788.60	0.401	209.88	2927.00	0.277	5.926	92.61	145.97	5.272	105.97	
	SD	22.657	26.657	131.783	1.538	0.4667	7.632	1615.544	0.0451	20.305	1617.838	0.1689	0.3472	36.179	1.998	0.5692	0.559	
4 mg/kg	05-072	173.0	32.0	87.0	22.2	9.63	77.7	552.0	0.37	173.1	997.0	0.13	5.60	47.8				short sample; no electrolytes
	05-078	144.0	41.0	92.0	26.2	10.17	85.5	578.0	0.40	178.1	1370.0	0.25	5.68	85.2	145.1	4.85	104.2	
	05-081	198.0	50.0	93.0	27.0	9.48	75.3	970.0	0.39	165.1	1535.0	0.13	5.58	54.4	144.4	5.45	107.9	
	05-090	143.0	97.0	296.0	24.0	10.64	72.6	2509.0	0.41	231.9	4196.0	0.33	5.62	112.2	145.9	6.19	105.8	hemolyzed; CK and LDH diluted 1:3
	05-094	177.0	56.0	105.0	25.4	9.90	79.8	1031.0	0.43	215.5	1431.0	0.25	5.83	51.2	146.1	5.49	106.1	
	05-095	120.0	57.0	331.0	26.0	10.04	85.6	3855.0	0.31	188.7	4885.0	0.92	6.18	125.9	148.4	6.13	106.7	hemolyzed; CK and LDH diluted 1:3
	05-105	201.0	83.0	359.0	24.0	10.70	88.7	4743.0	0.42	190.6	3794.0	0.28	5.92	69.3	149.5	5.54	106.4	CK and LDH diluted 1:3
	05-115	155.0	45.0	100.0	19.4	10.22	78.9	1205.0	0.30	180.9	1951.0	0.33	6.10	71.1	142.4	4.65	104.2	
	05-135	155.0	48.0	296.0	28.3	11.10	101.7	2546.0	0.39	212.6	3218.0	0.10	6.49	89.0	147.9	4.59	103.6	CK and LDH diluted 1:3
	05-136	*166.0*	*53.0*	*90.0*	*23.1*	*10.81*	*79.6*	*436.0*	*0.43*	*205.1*	*921.0*	*0.10*	*5.61*	*75.2*	*151.6*	*5.59*	*106.6*	
	Mean	163.20	56.20	184.90	23.56	10.269	82.54	1822.50	0.385	194.16	2429.80	0.284	5.861	78.04	146.81	5.387	105.72	
	SD	25.192	19.565	118.134	2.674	0.5311	8.348	1499.095	0.0462	21.353	1457.161	0.2423	0.3091	25.530	2.815	0.5855	1.424	
8 mg/kg	05-071	137.0	35.0	113.0	26.3	10.32	81.1	3239.0	0.39	176.6	1911.0	0.10	5.98	70.3	149.3	5.08	106.2	CK diluted 1:3; sample slightly hemolyzed
	05-074	146.0	50.0	352.0	23.3	10.65	65.1	2599.0	0.43	229.0	3425.0	0.10	5.61	37.1	144.5	6.17	106.5	slightly hemolyzed; CK and LDH diluted 1:3
	05-075	122.0	41.0	169.0	25.1	9.89	61.7	1702.0	0.34	171.3	2262.0	0.35	5.63	63.4	147.9	5.22	107.5	hemolyzed sample
	05-085	174.0	70.0	169.0	22.7	11.35	67.8	1039.0	0.50	234.3	1512.0	0.19	6.12	96.0	150.2	5.18	105.3	
	05-086	158.0	43.0	86.0	24.3	9.97	74.5	1041.0	0.42	193.6	1407.0	0.15	5.63	60.5	145.3	5.24	106.8	
	05-092	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	05-102	135.0	58.0	171.0	25.6	10.29	82.9	4739.0	0.34	167.7	3554.0	0.33	5.86	67.4	146.2	5.79	107.8	slightly hemolyzed; CK and LDH diluted 1:3
	05-106	192.0	55.0	234.0	24.6	9.84	76.6	2086.0	0.37	171.8	3355.0	0.41	6.25	80.4	146.0	5.14	105.4	CK and LDH diluted 1:3
	05-108	242.0	54.0	80.0	24.0	10.63	86.0	580.0	0.42	188.5	802.0	0.23	6.47	79.6	147.8	5.51	103.6	
	05-112	199.0	47.0	99.0	20.7	10.75	92.2	849.0	0.43	220.9	1038.0	0.20	5.89	104.9	143.2	4.16	103.1	
	Mean	167.22	50.33	163.67	24.87	10.410	76.43	1986.00	0.404	194.86	2148.67	0.229	5.938	72.29	146.71	5.277	105.86	
	SD	38.395	10.416	86.825	1.679	0.4895	10.171	1354.386	0.0588	26.455	1068.322	0.1115	0.3082	20.063	2.276	0.5516	1.423	
16 mg/kg	05-073	244.0	32.0	73.0	24.8	10.13	78.7	464.0	0.38	165.6	1361.0	0.10	5.81	109.9	145.2	5.41	104.0	
	05-083	144.0	515.0	971.0	27.2	10.26	77.3	4849.0	0.36	256.7	13637.0	0.34	5.87	116.7	145.6	8.45	104.9	slightly hemolyzed; CK diluted 1:3; LDH diluted 1:5
	05-091	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	05-109	163.0	50.0	262.0	21.9	10.57	73.8	1738.0	0.31	173.5	3742.0	0.38	6.06	105.1	144.2	5.41	106.0	CK and LDH diluted 1:3
	05-110	169.0	42.0	114.0	26.4	10.05	82.9	1216.0	0.35	180.1	1455.0	0.20	5.96	69.4	145.1	5.44	106.5	
	05-111	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	05-117	174.0	80.0	324.0	23.4	11.14	71.5	3876.0	0.41	231.1	4303.0	0.33	6.16	79.6	146.4	6.65	105.1	slightly hemolyzed; CK and LDH diluted 1:3
	05-130	171.0	74.0	349.0	20.2	10.26	85.3	2757.0	0.41	211.3	4583.0	0.35	6.04	92.9	143.9	5.82	103.7	CK and LDH diluted 1:3
	05-131	230.0	284.0	578.0	22.1	12.07	88.5	3698.0	0.39	267.1	7910.0	0.29	6.03	87.1	148.7	6.80	104.7	slightly hemolyzed; CK and LDH diluted 1:3
	05-132	133.0	101.0	484.0	22.5	11.07	77.3	10522.0	0.36	207.7	7870.0	0.59	6.39	130.9	143.1	6.33	104.3	sample hemolyzed; CK diluted 1:5; LDH diluted 1:3
	Mean	178.50	147.25	394.38	23.56	10.694	79.54	3640.00	0.371	211.64	5687.63	0.323	6.040	98.95	145.28	6.289	104.90	
	SD	38.932	168.940	288.016	2.396	0.6927	5.866	3145.126	0.0336	37.928	4077.827	0.1422	0.1795	20.410	1.729	1.0285	0.961	
32 mg/kg	05-080	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	05-082	185.0	52.0	246.0	25.9	10.90	68.8	2913.0	0.50	255.4	3165.0	0.19	5.65	58.3	147.0	7.03	104.5	CK and LDH diluted 1:3
	05-087	127.0	46.0	123.0	19.8	9.81	91.0	2633.0	0.31	166.6	2272.0	0.56	6.22	38.0	144.7	5.86	103.4	hemolyzed sample; CK diluted 1:3
	05-096	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	05-121	146.0	179.0	335.0	23.4	11.57	81.4	4773.0	0.40	280.4	5881.0	0.39	6.56	94.9	148.2	6.56	105.2	slightly hemolyzed; CK and LDH diluted 1:3
	05-122	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	05-123	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	05-124	161.0	59.0	227.0	22.3	10.83	87.8	1599.0	0.39	223.0	1826.0	0.24	5.91	61.8	143.2	4.89	104.6	slightly hemolyzed
	05-125	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	05-134	193.0	47.0	98.0	19.7	10.11	70.2	854.0	0.40	170.3	1298.0	0.10	5.66	37.0	141.4	5.17	105.8	
	Mean	162.40	76.60	205.80	22.22	10.644	79.84	2546.40	0.400	282.14	3888.40	0.296	6.000	58.00	144.90	5.902	104.70	
	SD	27.254	57.474	96.482	2.685	0.6961	10.864	1494.893	0.0675	37.238	1816.500	0.1812	0.3899	13.543	2.760	0.9038	0.894	
15 mg/kg	05-093	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	05-097	138.0	81.0	615.0	28.5	10.20	81.5	8220.0	0.38	193.9	8014.0	0.71	6.34	117.9	145.9	6.98	105.9	hemolyzed sample; CK diluted 1:5; LDH diluted 1:3
	05-099	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	05-104	154.0	62.0	306.0	21.7	10.59	78.9	5652.0	0.38	178.3	4684.0	0.46	6.53	95.7	150.6	5.80	104.4	CK and LDH diluted 1:3
	05-107	167.0	49.0	139.0	25.6	10.99	86.8	1658.0	0.44	196.9	1394.0	0.34	6.43	109.7	145.1	6.17	104.2	
	05-113	205.0	51.0	133.0	24.1	10.93	91.5	1134.0	0.41	222.1	1524.0	0.21	6.31	159.8	146.4	4.73	103.9	
	05-116	118.0	55.0	208.0	23.2	11.57	78.1	5750.0	0.29	246.4	3916.0	0.54	6.36	84.4				short sample; no electrolytes
	05-126	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	05-129	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	
	05-133	202.0	37.0	78.0	23.4	10.83	75.0	808.0	0.37	212.2	895.0	0.18	5.94	85.4	145.8	4.90	105.9	
	Mean	164.40	55.83	246.50	24.42	10.852	81.97	3902.33	0.378	208.30	3437.83	0.407	6.318	108.82	146.76	5.716	104.86	
	SD	34.716	14.811	196.797	2.369	0.4549	6.121	3164.271	0.0504	24.861	2741.671	0.2035	0.2013	28.281	2.196	0.9286	0.966	

No data
(f) = Animal died on study

APPENDIX T

SUMMARY OF 90-DAY HEMATOLOGY AND INDIVIDUAL HEMATOLOGY DATA

Table T-1
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Summary of Hematology
Male Rats

Period		Methylcellulose Control	RDX in 1% Methylcellulose / 0.2% Tween 80				
			4 mg/kg	8 mg/kg	10 mg/kg	12 mg/kg	15 mg/kg
WBC	Mean	7.682	7.298	6.755	7.107	7.744	7.435
(K/uL)	S.D.	2.3632	1.5585	2.9272	1.7081	1.9382	1.6905
	N	9	9	8	7	7	6
NEU	Mean	14.989	11.922	12.438	12.757	12.857	19.033
(%N)	S.D.	3.7049	1.4695	2.4260	1.4339	2.8278	5.1821
	N	9	9	8	7	7	6
LYM	Mean	74.056	80.478	78.700	76.457	75.543	74.633
(%L)	S.D.	13.1986	4.0084	6.7764	8.0025	5.4030	6.1461
	N	9	9	8	7	7	6
MONO	Mean	4.998	4.237	3.326	4.823	5.470	3.695
(%M)	S.D.	5.5678	2.0856	1.0513	3.2626	3.5247	1.5259
	N	9	9	8	7	7	6
EOS	Mean	1.0702	0.8273	0.9005	0.9996	0.7607	0.7822
(%E)	S.D.	0.39674	0.24849	0.19751	0.66194	0.27551	0.11868
	N	9	9	8	7	7	6
BASO	Mean	4.886	2.543	4.621	4.969	5.371	1.865
(%B)	S.D.	6.0952	1.0605	5.3092	4.9074	4.2227	0.4732
	N	9	9	8	7	7	6
RBC	Mean	8.567	8.643	7.943	8.381	8.201	8.115
(M/uL)	S.D.	0.1812	0.3167	1.2146	0.4183	0.7827	0.7584
	N	9	9	8	7	7	6
HGB	Mean	15.02	14.92	14.21	14.99	14.86	14.07
(g/dL)	S.D.	0.587	0.779	2.137	0.701	0.980	1.297
	N	9	9	8	7	7	6
HCT	Mean	32.92	33.61	31.29	33.06	32.50	31.60
(%)	S.D.	0.761	1.214	4.587	1.516	2.733	2.522
	N	9	9	8	7	7	6
MCV	Mean	38.41	38.88	39.44*	39.44*	39.69*	38.97
(fL)	S.D.	0.511	0.499	0.605	0.496	0.958	0.750
	N	9	9	8	7	7	6
MCH	Mean	17.52	17.26	17.89	17.89	18.23	17.37
(pg)	S.D.	0.474	0.617	0.452	0.402	1.467	0.476
	N	9	9	8	7	7	6
MCHC	Mean	45.61	44.38	45.38	45.33	45.89	44.58
(g/dL)	S.D.	1.263	1.385	1.001	0.668	3.398	1.038
	N	9	9	8	7	7	6
RDW	Mean	17.04	17.26	16.40	16.60	16.43	16.97
(%)	S.D.	0.871	0.652	1.533	0.748	1.016	0.207
	N	9	9	8	7	7	6
PLT	Mean	420.17	509.00	467.33	476.43	388.30	562.83
(K/uL)	S.D.	270.428	201.009	206.822	291.380	302.010	244.627
	N	9	9	8	7	7	6
MPV	Mean	8.080	7.717	7.721	7.814	7.548	7.407
(fL)	S.D.	0.5017	0.2158	0.4647	0.3688	0.1696	0.2949
	N	7	9	8	7	4	6
AVG. PT	Mean	15.100	13.383	13.420	15.800	14.560	14.067
(sec)	S.D.	1.6716	0.6369	0.2588	2.8071	3.2478	0.6976
	N	8	6	5	6	5	6
AVG. APTT.	Mean	14.657	15.217	17.780	16.500	14.260	15.967
(sec)	S.D.	2.9137	3.3187	4.2868	1.7795	1.0550	3.8151
	N	7	6	5	4	5	6

* p less than or equal to 0.05
ANOVA with Holm-Sidak Method

Table T-2
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Summary of Hematology
Female Rats

Period		Methylcellulose Control	RDX in 1% Methylcellulose / 0.2% Tween 80 4 mg/kg	8 mg/kg	10 mg/kg	12 mg/kg	15 mg/kg
WBC	Mean	4.541	5.523	6.600	5.080	6.886	5.838
(K/uL)	S.D.	2.4127	1.1302	2.6138	2.4285	3.5271	2.3798
	N	8	10	9	5	5	6
NEU	Mean	12.418	7.831	8.564	10.972	10.378	12.692
(%N)	S.D.	12.8596	1.7607	2.2374	1.3638	3.051	10.6694
	N	8	10	9	5	5	6
LYM	Mean	72.450	83.420	84.522	81.180	80.780	81.283
(%L)	S.D.	24.5700	3.9913	6.3253	3.5787	5.3616	11.9005
	N	8	10	9	5	5	6
MONO	Mean	10.930	3.962	3.667	4.907	5.012	3.692
(%M)	S.D.	10.5359	2.2616	2.9318	3.5112	3.1995	1.4764
	N	8	10	9	5	5	6
EOS	Mean	1.2220	0.5805	0.5653	0.8912	0.8772	0.7020
(%E)	S.D.	1.57026	0.17543	0.19035	0.21448	0.56175	0.50141
	N	8	10	9	5	5	6
BASO	Mean	2.999	4.211	2.666	2.094	2.958	1.650
(%B)	S.D.	2.3977	4.3044	3.1669	1.0057	1.7697	0.6421
	N	8	10	9	5	5	6
RBC	Mean	7.643	7.866	7.873	7.532	7.830	7.448
(M/uL)	S.D.	0.4780	0.1884	0.3735	0.1695	0.2223	0.7443
	N	8	10	9	5	5	6
HGB	Mean	13.988	14.29	14.600	13.840	14.660	13.417
(g/dL)	S.D.	0.8626	0.7520	0.723	0.2702	0.5030	1.3152
	N	8	10	9	5	5	6
HCT	Mean	31.49	32.39	32.89	31.54	32.82	30.88
(%)	S.D.	2.047	0.817	1.370	0.371	0.756	2.733
	N	8	10	9	5	5	6
MCV	Mean	41.23	41.15	41.82	41.92*	41.90*	41.47
(fL)	S.D.	0.396	0.172	0.517	0.593	0.520	0.596
	N	8	10	9	5	5	6
MCH	Mean	18.30	18.15	18.56	18.40	18.68	18.03
(pg)	S.D.	0.278	0.800	0.364	0.235	0.432	0.985
	N	8	10	9	5	5	6
MCHC	Mean	44.43	44.11	44.36	43.86	44.58	43.48
(g/dL)	S.D.	0.680	1.985	0.750	0.764	1.316	2.474
	N	8	10	9	5	5	6
RDW	Mean	14.70	14.76	15.43	14.58	14.72	14.68
(%)	S.D.	0.934	0.845	0.500	0.342	0.920	1.050
	N	8	10	9	5	5	6
PLT	Mean	305.87	325.40	429.30	451.44	408.68	197.45
(K/uL)	S.D.	254.027	316.925	323.818	343.780	338.221	290.139
	N	8	10	9	5	5	6
MPV	Mean	8.048	8.206	7.744	8.006	8.188	7.667
(fL)	S.D.	0.4254	0.8554	0.1628	0.5077	0.7550	0.2281
	N	6	7	7	5	5	3
AVG. PT	Mean	N/A	14.25	18.13	14.60	17.05	19.40
(sec)	S.D.	N/A	0.636	3.946	0.283	1.930	N/A
	N	0	2	3	2	4	1
AVG. APTT.	Mean	N/A	15.20	13.55	15.350	17.77	13.90
(sec)	S.D.	N/A	4.525	3.323	10.394	7.050	N/A
	N	0	2	2	2	3	1

* p less than or equal to 0.05
ANOVA with Holm-Sidak Method

Table T-3
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

90-Day Individual Hematology
Male Rats

Group	Animal ID	WBC (K/uL)	NEU (%N)	LYM (%L)	MONO (%M)	EOS (%E)	BASO (%B)	RBC (M/uL)	HGB (g/dL)	HCT (%)	MCV (fL)	MCH (pg)	MCHC (g/dL)	RDW (%)	PLT (K/uL)	MPV (fL)	AVG. PT (sec)	AVG. APTT. (sec)
Methylcellulose Control	05-011	7.44	11.70	84.30	1.50	0.577	1.96	8.27	14.2	31.7	38.4	17.2	44.8	16.0	40.8	9.03	17.6	
	05-012	10.40	14.50	80.00	2.73	1.000	1.83	8.53	14.9	32.5	38.1	17.4	45.7	18.1	594.0	7.74	13.9	15.3
	05-016																	
	05-020	8.31	12.20	83.20	2.32	0.741	1.55	8.50	15.1	33.6	39.5	17.7	44.9	17.0	624.0	7.64	13.4	17.1
	05-023	7.87	12.60	82.70	2.52	0.840	1.36	8.79	15.5	33.2	37.7	17.7	46.8	18.5	593.0	8.42	14.2	15.7
	05-052	6.62	13.70	80.40	3.10	0.787	1.97	8.62	15.1	33.5	38.8	17.5	45.2	17.0	592.0	7.66	15.1	10.9
	05-060	11.00	12.80	59.10	7.98	1.560	18.50	8.67	15.0	33.4	38.5	17.3	44.9	16.7	530.0	8.07		
	05-064	4.90	20.80	71.30	3.12	1.650	3.10	8.73	14.8	33.3	38.2	16.9	44.3	16.1	57.8		16.4	14.0
	05-066	3.74	21.70	45.90	19.00	1.500	11.90	8.31	14.4	31.7	38.1	17.4	45.5	16.4	89.9		16.9	11.0
	05-070	8.86	14.90	79.60	2.71	0.977	1.80	8.68	16.2	33.4	38.4	18.6	48.4	17.6	660.0	8.00	13.3	18.6
	Mean	**7.682**	**14.989**	**74.056**	**4.998**	**1.0702**	**4.886**	**8.567**	**15.02**	**32.92**	**38.41**	**17.52**	**45.61**	**17.04**	**420.17**	**8.000**	**15.100**	**14.657**
	SD	**2.3632**	**3.7049**	**13.1986**	**5.5678**	**0.39674**	**6.0952**	**0.1812**	**0.587**	**0.761**	**0.511**	**0.474**	**1.263**	**0.871**	**270.428**	**0.5017**	**1.6716**	**2.9137**
4 mg/kg	05-001	6.11	12.30	84.80	1.29	0.601	1.02	8.48	14.4	32.5	38.4	17.0	44.3	16.5	607.0	7.93	12.6	9.6
	05-007	6.23	13.40	74.90	7.70	0.646	3.40	8.51	13.5	32.7	38.4	15.9	41.2	17.6	680.0	7.75	13.3	16.5
	05-013																	
	05-028	7.59	11.10	82.90	3.87	0.722	1.34	8.70	15.1	33.7	38.7	17.4	44.9	16.9	667.0	7.47	13.7	17.5
	05-033	10.20	10.80	81.60	3.70	1.150	2.75	8.93	16.1	35.1	39.3	18.0	45.8	17.8	233.0	7.81		
	05-039	8.39	11.90	76.50	6.66	1.020	3.93	8.95	15.2	34.5	38.5	16.9	44.0	18.4	651.0	7.80		
	05-041	7.18	10.50	84.20	2.28	1.240	1.78	8.49	15.0	32.7	38.5	17.6	45.8	16.4	272.0	7.94	13.8	18.1
	05-055	7.70	12.20	80.00	4.61	0.554	2.67	9.11	15.8	35.4	38.9	17.3	44.6	17.6	656.0	7.32	14.2	16.8
	05-062	4.67	14.80	75.20	5.38	0.792	3.87	8.07	14.4	32.0	39.6	17.8	45.0	17.2	228.0	7.86		
	05-067	7.61	10.30	84.20	2.64	0.721	2.13	8.55	14.8	33.9	39.6	17.4	43.8	16.9	585.0	7.57	12.7	12.8
	Mean	**7.298**	**11.922**	**80.478**	**4.237**	**0.8273**	**2.543**	**8.643**	**14.92**	**33.61**	**38.88**	**17.26**	**44.38**	**17.26**	**509.00**	**7.717**	**13.383**	**15.217**
	SD	**1.5585**	**1.4695**	**4.0084**	**2.0856**	**0.24849**	**1.0605**	**0.3167**	**0.779**	**1.214**	**0.499**	**0.617**	**1.385**	**0.652**	**201.009**	**0.2158**	**0.6369**	**3.3187**
8 mg/kg	05-003	5.20	10.90	82.80	3.57	0.778	1.91	8.25	15.1	33.0	39.9	18.3	45.9	15.4	609.0	7.42	13.7	15.2
	05-006	9.22	14.00	81.70	1.62	0.890	1.80	7.75	13.9	31.0	40.1	17.9	44.7	16.0	215.0	8.14		
	05-015	1.67	14.20	64.60	4.20	1.190	15.80	5.07	9.2	20.4	40.3	18.1	44.9	13.4	96.6	8.56		
	05-034	9.67	15.50	77.60	4.46	0.627	1.77	8.95	15.5	35.2	39.3	17.3	44.0	16.7	653.0	7.07	13.7	20.1
	05-037	7.37	8.30	87.10	2.41	0.873	1.35	8.31	15.4	32.8	39.4	18.5	46.8	17.8	420.0	7.78	13.2	13.0
	05-045	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-046	3.68	10.10	74.70	4.44	0.954	9.75	8.08	13.9	31.3	38.7	17.2	44.5	17.2	395.0	7.66	13.3	16.7
	05-051	8.18	13.20	81.60	2.53	1.160	1.56	8.56	15.4	33.2	38.8	18.0	46.5	18.3	607.0	7.39	13.2	23.9
	05-068	9.05	13.30	79.50	3.38	0.732	3.03	8.57	15.3	33.4	39.0	17.8	45.7	16.4	543.0	7.75		
	05-069																	
	Mean	**6.755**	**12.438**	**78.700**	**3.326**	**0.9005**	**4.621**	**7.943**	**14.21**	**31.29**	**39.44**	**17.89**	**45.38**	**16.40**	**467.33**	**7.721**	**13.420**	**17.780**
	SD	**2.9272**	**2.4260**	**6.7764**	**1.0513**	**0.19751**	**5.3092**	**1.2146**	**2.137**	**4.587**	**0.605**	**0.452**	**1.001**	**1.533**	**206.822**	**0.4647**	**0.2588**	**4.2868**
10 mg/kg	05-017	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-024	6.61	14.10	81.00	2.82	0.434	1.69	7.93	14.2	31.3	39.5	17.9	45.2	17.0	906.0	7.50	16.8	
	05-040	9.78	11.70	62.30	9.55	1.950	14.50	8.48	15.7	33.8	39.8	18.5	46.4	16.2	104.0	8.09	13.9	18.3
	05-042	5.29	13.10	82.50	2.19	0.552	1.64	8.73	15.0	33.7	38.6	17.2	44.6	16.4	671.0	7.35	13.5	17.2
	05-049	7.81	11.40	72.70	6.68	0.586	8.66	7.87	14.1	31.0	39.4	18.0	45.6	15.7	435.0	8.10		
	05-050	7.60	15.00	71.10	7.96	1.940	4.02	8.71	15.7	34.2	39.2	18.0	45.9	17.7	656.0	7.42	12.8	16.4
	05-053	4.77	12.80	84.10	0.80	0.913	1.35	8.07	14.6	32.4	40.2	18.0	44.9	15.9	143.0	8.09	19.7	14.1
	05-054	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-056	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-065	7.89	11.20	81.50	3.76	0.622	2.92	8.88	15.6	35.0	39.4	17.6	44.7	17.3	420.0	8.15	18.1	
	Mean	**7.187**	**12.757**	**76.457**	**4.823**	**0.9996**	**4.969**	**8.381**	**14.99**	**33.06**	**39.46**	**17.89**	**45.33**	**16.60**	**476.43**	**7.814**	**15.800**	**16.500**
	SD	**1.7081**	**1.4339**	**8.0025**	**3.2626**	**0.66194**	**4.9074**	**0.4183**	**0.701**	**1.516**	**0.496**	**0.402**	**0.668**	**0.748**	**291.380**	**0.3688**	**2.8071**	**1.7795**
12 mg/kg	05-005	7.32	10.10	73.40	3.51	0.371	12.60	7.36	13.0	29.2	39.7	17.7	44.6	14.7	15.8			
	05-009	7.59	12.90	80.40	3.73	0.535	2.49	7.81	14.1	31.5	40.4	18.1	44.7	16.2	609.0	7.64	13.1	15.7
	05-019	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-021	3.67	13.40	71.20	7.38	0.843	7.19	7.17	15.3	28.7	40.1	21.4	53.3	17.0	159.0		20.3	13.5
	05-027																	
	05-031	9.25	10.20	67.00	12.80	1.080	8.84	8.85	15.1	35.4	40.0	17.1	42.7	15.9	33.3		12.5	14.7
	05-047	8.46	18.50	75.30	3.42	0.734	2.01	8.19	15.1	33.4	40.8	18.4	45.1	16.5	653.0	7.41	13.9	13.0
	05-048	8.95	13.10	80.10	3.71	1.120	1.99	8.96	15.7	34.7	38.7	17.6	45.4	16.7	627.0	7.74	13.0	14.4
	05-058	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-063	8.97	11.80	81.40	3.74	0.642	2.48	9.07	15.7	34.6	38.1	17.3	45.4	18.0	621.0	7.40		
	Mean	**7.744**	**12.857**	**75.543**	**5.470**	**0.7607**	**5.371**	**8.201**	**14.86**	**32.50**	**39.69**	**18.23**	**45.89**	**16.43**	**388.30**	**7.548**	**14.560**	**14.260**
	SD	**1.9382**	**2.8278**	**5.4030**	**3.5247**	**0.27551**	**4.2227**	**0.7827**	**0.980**	**2.733**	**0.958**	**1.467**	**3.398**	**1.016**	**302.810**	**0.1696**	**3.2478**	**1.0550**
15 mg/kg	05-008	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-010	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-018	6.26	17.70	75.50	4.10	0.783	1.90	8.58	15.1	33.0	38.4	17.6	45.9	17.0	631.0	7.80	13.9	9.0
	05-022	9.73	18.30	75.00	3.78	0.855	2.05	8.58	14.5	32.7	38.1	16.9	44.5	17.2	683.0	7.26	13.8	19.6
	05-025	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-030	9.11	14.50	80.30	2.87	0.839	1.51	8.65	14.8	33.3	38.5	17.2	44.6	16.8	659.0	7.51	13.5	17.5
	05-032	6.37	14.50	81.70	1.77	0.811	1.22	8.52	14.7	33.4	39.2	17.3	44.2	16.7	174.0	7.55	14.2	18.5
	05-035																	
	05-043	5.52	20.80	69.70	6.33	0.547	2.60	7.53	13.7	30.1	40.0	18.2	45.4	17.2	376.0	7.39	13.6	14.6
	05-057	7.62	28.40	65.60	3.32	0.858	1.91	6.83	11.6	27.1	39.6	17.0	42.9	16.9	854.0	6.93	15.4	16.6
	Mean	**7.435**	**19.033**	**74.633**	**3.695**	**0.7822**	**1.865**	**8.115**	**14.07**	**31.60**	**38.97**	**17.37**	**44.58**	**16.97**	**562.83**	**7.407**	**14.067**	**15.967**
	SD	**1.6905**	**5.1821**	**6.1461**	**1.5259**	**0.11868**	**0.4732**	**0.7584**	**1.297**	**2.522**	**0.750**	**0.476**	**1.038**	**0.207**	**244.627**	**0.2949**	**0.6976**	**3.8151**

No data
(f) = Animal died on study

Table T-4
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

90-Day Individual Hematology
Female Rats

Dose	Animal ID	WBC (K/uL)	NEU (%N)	LYM (%L)	MONO (%M)	EOS (%E)	BASO (%B)	RBC (M/uL)	HGB (g/dL)	HCT (%)	MCV (fL)	MCH (pg)	MCHC (g/dL)	RDW (%)	PLT (K/uL)	MPV (fL)	AVG. PT (sec)	AVG. APTT. (sec)
Methylcellulose Control	05-076	0 38	43 80	16 40	31 40	5 060	3 42	7.80	13 90	32 2	41 3	17 9	43 3	16 0	330 0	8 43		
	05-077	8 86	7 33	61 40	22 60	0 652	8.02	8 16	15 10	34 2	42.0	18 5	44 0	15.0	128 0	8 10		
	05-084	4 96	9 21	79 80	8 39	0 846	1.81	8.07	14 70	33 2	41.2	18 3	44 4	15.2	263 0	8 03		
	05-088	3 35	3 60	93 00	1 46	0.403	1 50	7 04	13.20	29 2	41 5	18 7	45 2	14.0	9 3			
	05-098	3 26	8 54	82.60	5 84	1 050	2.02	6 87	12 40	28 1	41.0	18 0	43 9	12 9	11 7			
	05-100																	
	05-101																	
	05-114	5 32	6 71	88 60	2 49	0 350	1 83	7 50	13 90	30 9	41.2	18 5	45.1	15.0	419 0	7.30		
	05-120	4 72	9.75	83 30	5 79	0 516	0 61	7 68	14.20	31 4	40.8	18 4	45 1	14.4	682 0	7.95		
	05-127	5 48	10.40	74 50	9 47	0 899	4 78	8 02	14.50	32 7	40 8	18 1	44 4	15 1	604 0	8 48		
	Mean	**4.541**	**12.418**	**72.450**	**10.930**	**1.2120**	**2.999**	**7.643**	**13.988**	**31.49**	**41.23**	**18.30**	**44.43**	**14.70**	**305.87**	**8.048**		
	SD	**2.4127**	**12.8596**	**24.5700**	**10.5359**	**1.57026**	**2.3977**	**0.4780**	**0.8626**	**2.047**	**0.396**	**0.278**	**0.680**	**0.934**	**254.027**	**0.4254**		
4 mg/kg	05-072	5 63	9 02	84.60	4 23	0 715	1 39	8 07	15 00	33 4	41 4	18.6	44 9	15 8	734 0	7 44	14 7	12 0
	05-078	6 12	4 31	80 50	2 22	0 551	12 40	7 77	14 10	31 9	41 0	18 1	44.2	15 0	12 3			
	05-081	3 79	6 45	85 60	5 12	0 269	2 54	8.12	15 10	33 5	41 2	18 6	45 1	15.6	66 3			
	05-090	4 98	10.00	82 30	3 49	0.371	3.82	7 83	12 60	32 4	41.3	16 0	38.8	15 7	340 0	7 53		
	05-094	4.92	7 83	83 70	5 68	0 723	2 08	7 76	14 10	32 1	41 4	18 1	43.8	14 6	660 0	7 86		
	05-095	6 48	7 84	88 70	1 30	0 605	1 59	7 55	13.60	31.0	41 1	18 1	43 9	14.6	79 1	8 65		
	05-105	4 08	6 56	76 50	4 06	0.779	12.10	7.99	14 80	32.8	41.0	18 5	45.1	14 9	16 5			
	05-115	5.24	9 88	85 00	2 21	0 425	2.53	7 66	14 30	31.5	41 1	18 7	45 4	14.4	38 8	9 85		
	05-135	6 83	9 04	78 70	9 01	0 759	2 53	8 05	14 60	33 1	41.1	18 1	44 1	13 9	598 0	8 43		
	05-136	7 16	7 38	88 60	2 30	0.608	1.13	7 86	14 70	32.2	40 9	18.7	45.8	13.1	709 0	7 68	13 8	18 4
	Mean	**5.523**	**7.831**	**83.420**	**3.962**	**0.5805**	**4.211**	**7.866**	**14.290**	**32.39**	**41.15**	**18.15**	**44.11**	**14.76**	**325.40**	**8.206**	**14.25**	**15.20**
	SD	**1.1302**	**1.7607**	**3.9913**	**2.2616**	**0.17543**	**4.3044**	**0.1884**	**0.7520**	**0.817**	**0.172**	**0.800**	**1.985**	**0.845**	**316.925**	**0.8554**	**0.636**	**4.525**
8 mg/kg	05-071	6 29	8 53	86.60	2.07	0 570	2 19	7 89	14 40	32.5	41 2	18.2	44.2	15 3	512 0	7.96		
	05-074	8 24	8.36	86 40	1.94	0 671	2 60	8 02	15 00	33 0	41 1	18.7	45 4	15 3	486 0	7 82		
	05-075	4 13	7.45	88 90	1.82	0.287	1 54	7 88	14 40	33 0	41 9	18.3	43 6	15 7	20 1	7 85		
	05-085	11 70	4 68	92 20	1 11	0 450	1 53	8.48	16 00	35 3	41.7	18.8	45 2	15 7	25.5		20 0	15 9
	05-086	5 33	10 30	79 60	8 04	0 468	1 61	7 31	14 00	31 3	42.8	19 2	44 8	15 2	822 0	7 84		
	05-092	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-102	4.91	7.62	89 60	1 35	0 347	1.11	8 14	15.20	34.0	41.8	18 7	44.7	15.8	606 0	7.64		
	05-106	3 74	8 35	73 20	6 59	0 814	11 00	7 37	13 50	30 8	41 9	18 4	43 9	15 0	12 1			
	05-108	5.89	13 00	77 40	7 91	0 802	0 89	8 09	14 50	33 7	41.7	18 0	43 1	16.3	728 0	7 55	20 8	
	05-112	9 17	8 79	86 80	2 17	0 679	1.53	7.68	14 40	32 4	42 3	18 7	44 3	14.6	652 0	7.55	13 6	11 2
	Mean	**6.600**	**8.564**	**84.522**	**3.667**	**0.5653**	**2.666**	**7.873**	**14.600**	**32.89**	**41.82**	**18.56**	**44.36**	**15.43**	**429.30**	**7.744**	**18.13**	**13.55**
	SD	**2.6138**	**2.2374**	**6.3253**	**2.9318**	**0.19035**	**3.1669**	**0.3735**	**0.7228**	**1.370**	**0.517**	**0.364**	**0.750**	**0.500**	**323.818**	**0.1628**	**3.946**	**3.323**
10 mg/kg	05-073	5 40	13 20	78.50	6 14	0.817	1.39	7.35	13.40	31 3	42.6	18.3	42 9	14 3	713 0	7 57	14.8	22 7
	05-083	3 07	11.00	83 10	2 40	1.210	2 36	7 76	14 10	31.8	41 0	18.2	44 3	14 3	85 4	7 96		
	05-091	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-109																	
	05-110	3 73	10 80	79 10	5 52	0 943	3 71	7.39	13 90	31 0	42 0	18 8	44.8	14.4	669 0	7.58	14 4	8 0
	05-111	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-117																	
	05-130																	
	05-131	4 05	9 56	78 60	9 76	0 866	1.21	7 53	13.80	31 8	42 2	18 3	43.3	14.9	724 0	8 11		
	05-132	9 15	10 30	86 60	0 71	0.620	1.80	7 63	14 00	31.8	41 8	18 4	44 0	15 0	65 8	8 81		
	Mean	**5.080**	**10.972**	**81.180**	**4.907**	**0.8912**	**2.094**	**7.532**	**13.840**	**31.54**	**41.92**	**18.40**	**43.86**	**14.58**	**451.44**	**8.006**	**14.60**	**15.35**
	SD	**2.4285**	**1.3638**	**3.5787**	**3.5112**	**0.21448**	**1.0057**	**0.1695**	**0.2702**	**0.371**	**0.593**	**0.235**	**0.764**	**0.342**	**343.780**	**0.5077**	**0.283**	**10.394**
12 mg/kg	05-080	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-082	9 59	12 70	81 10	2 82	1 230	2 19	7 88	15 00	33 0	41 8	19 0	45 4	15 6	652 0	7 81	17 9	
	05-087	3 42	14 40	73 80	7 98	0.247	3 53	7.64	13.90	32.7	42 8	18 1	42 4	13 9	34.9	8 77	17 0	25 9
	05-096	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-121	4.46	7.39	77 30	8 87	0 633	5 78	8.18	15.20	34 0	41 6	18.6	44.7	13 9	41 5	9 21	18 9	13 4
	05-122	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-123	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-124	11 60	9.30	87 00	1.77	0.616	1.33	7.81	14.50	32.4	41.5	18 5	44 6	15 8	655 0	7 54		
	05-128	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-134	5 36	8 10	84 70	3 62	1 660	1 96	7.64	14.70	32 0	41 8	19 2	45 8	14 4	660 0	7.61	14 4	14 0
	Mean	**6.886**	**10.378**	**80.780**	**5.012**	**0.8772**	**2.958**	**7.830**	**14.660**	**32.82**	**41.90**	**18.68**	**44.58**	**14.72**	**408.68**	**8.188**	**17.05**	**17.77**
	SD	**3.5271**	**3.0351**	**5.3616**	**3.1995**	**0.56175**	**1.7697**	**0.2223**	**0.5030**	**0.756**	**0.520**	**0.432**	**1.316**	**0.920**	**338.221**	**0.7550**	**1.930**	**7.050**
15 mg/kg	05-093	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-097	9 90	10 10	86 50	1 64	0 637	1 10	8 36	15 80	33.9	40.5	18.9	46 6	15 4	769 0	7 54		
	05-099	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-104	6 72	7 07	88 70	2 29	0 260	1 73	7 11	13 00	30 0	42.1	18.3	43 5	14 1	15 9			
	05-107	3 91	6 69	87 80	3 95	0 230	1 34	6 35	11 80	26 6	41 8	18 5	44 2	13 8	26 8			
	05-113	3 57	34 30	57 40	3 91	1.540	2 88	7 17	13 10	30.1	41 9	18.3	43 6	14 1	21 0			
	05-116	4 49	8 45	84 60	4 88	0.525	1 57	8 18	13.20	33.8	41 4	16.1	39.0	16 5	183 0	7 93		
	05-126	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-129	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	05-133	6.44	9 54	82 7	5 48	1 020	1 28	7.52	13 6	30.9	41.1	18 1	44 0	14 2	169 0	7 53	19 4	13 9
	Mean	**5.838**	**12.691**	**81.283**	**3.691**	**0.7020**	**1.650**	**7.448**	**13.417**	**30.88**	**41.47**	**18.03**	**43.48**	**14.68**	**197.45**	**7.667**	**19.40**	**13.90**
	SD	**2.3798**	**10.6694**	**11.9005**	**1.4764**	**0.50141**	**0.6421**	**0.7443**	**1.3152**	**2.733**	**0.596**	**0.985**	**2.474**	**1.050**	**290.139**	**0.2281**		

No data
(f) = Animal died on study

APPENDIX U

HISTOPATHOLOGY REPORT

Table U-1
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Summary of Histopathological Findings - Males

			Incidence / No. Examined	
Tissue	Finding	Severity	Methylcellulose Control	15 mg/kg RDX
Adrenal Cortex	Extracapsular cortical nodule		1/10	0/8
Bone, Skull	Hemorrhage, focal	Mild	0/10	1/7
Epididymis	Inflammation, subacute	Minimal	0/10	1/8
Esophagus	Degeneration, muscularis, focal	Mild	0/10	1/8
Eye	Dystrophy, cornea	Minimal	6/10	7/8
		Mild	2/10	0/8
Eye	Microgranuloma, conjuntiva	Minimal	2/10	1/8
			1/10	0/8
	Mineralization, artery	Mild	2/10	2/8
		Moderate	0/10	1/8
Heart	Cardiomyopathy	Minimal	1/10	2/8
		Mild	1/10	1/8
	Congestion	Moderate	0/10	1/8
	Epicarditis	Minimal	1/10	0/8
	Mineralization, artery		0/10	1/8
Kidney	Congestion	Mild	0/10	1/8
	Intratubular proteinic material	Minimal	1/10	0/8
	Microconcretion	Minimal	1/10	0/8
	Regeneration, tubular	Minimal	4/10	3/8
Larynx	Inflammation, subacute	Mild	0/10	2/7
	Microgranuloma	Minimal	1/9	0/8
Liver	Congestion	Mild	0/10	1/8
	Inflammation, acute, focal	Minimal	1/10	0/8
Lungs	Congestion	Mild	0/10	1/8
	Edema	Moderate	0/10	1/8
	Hemorrhage	Minimal	2/10	1/8
		Mild	1/10	0/8
Lymph Node, Mandibular	Sequestered blood	Mild	2/10	0/8
Lymph Node, Mediastinal	Sequestered blood	Minimal	1/10	0/8
		Mild	2/10	0/8
Lymph Node, Mesenteric	Hemorrhage	Minimal	1/10	0/8
Lymph Node, Pancreatic	Sequestered blood	Mild	1/10	0/8
Mediastinum	Inflammation, chronic, focal	Mild	0/10	1/8
Prostate	Inflammation, subacute	Mild	0/10	1/8
Skin	Infiltration, histiocytic	Minimal	1/10	0/8
Subcutis	Mineralization, artery	Mild	2/10	1/8
Testis	Hypospermatogenesis, unilateral	Moderate	0/10	1/8
	Mineralization, unilateral	Mild	0/10	1/8
Thymus	Hemorrhage	Minimal	2/10	3/8
		Mild	0/10	2/8
Thyroid	Embryonic remnant		1/9	1/7
Tongue	Mineralization, artery	Mild	7/9	5/8
		Moderate	2/9	2/8

Table U-2
Protocol No. 5131-38-02-12-01
Subchronic Oral Toxicity of RDX in Rats

Summary of Histopathological Findings - Females

			Incidence / No. Examined	
Tissue	Finding	Severity	Methylcellulose Control	15 mg/kg RDX
Eye	Dystrophy, cornea	Minimal	5/10	4/6
	Microgranuloma, conjuntiva	Minimal	3/10	
	Mineralization, artery	Minimal	1/10	
		Mild		1/6
		Moderate	1/10	
Heart	Cardiomyopathy	Minimal		1/6
Kidney	Microconcretion	Minimal	6/10	4/6
		Mild	1/10	
	Mineralization, artery	Minimal		1/6
	Regeneration, tubular	Minimal		1/6
Liver	Cytoplasmic alteration, basophilic, focal	Moderate		1/6
	Inflammation, acute, focal	Minimal		
Lungs	Hemorrhage	Minimal	2/10	2/6
Lymph Node, Mandibular	Sequestered blood	Minimal		1/6
		Mild	1/10	2/6
Ovary	Parovarian cyst			1/6
Pituitary	Embryonic remnant			1/4
Spleen	Fibrosis, capsular			1/6
Thymus	Hemorrhage	Minimal	3/10	3/6
Thyroid	Embryonic remnant		1/10	
Tongue	Mineralization, artery	Minimal	1/10	3/6
		Mild	6/10	3/6
Uterus	Dilatation	Mild	2/10	1/6
		Moderate		1/6

APPENDIX V

NEUROTOXICITY DATA

NEUROTOXICITY SUMMARY
TOXICOLOGICAL STUDY NO. 85-MA-5131-02
PROTOCOL NO. 5131-38-02-12-01
SUBHCRONIC ORAL TOXICITY OF RDX IN RATS

Behavioral Testing

All rats were tested using a functional observation battery (FOB) which is consistent with the procedure outlined by Moser (2000). This battery consisted of weekly home cage, hand-held, open arena observations. After week 11, elicited responses and motor activity monitoring evaluations were made.

Methods

Each rat was observed in the home cage. The observer scored the rat on its posture as well as the presence and absence of convulsions or tremors. If either tremors or convulsions were present, they were scored further for severity. The rat was also scored on its level of agitation. Any observations that could be made without disturbing the rat were made, e.g. salivation and barbering.

Each rat was removed to a separate lab (Rm 3014) for the hand-held and open arena observations. Each rat was scored on reactivity to removal from the cage and reactivity to handling. The observer then scored for the presence or absence of lacrimation, salivation, piloerection, palpebral closure, skin condition, condition of eyes and nose and exophthalmus. Pupillary status was also noted. Next, the rat was place in the center of an open arena (60x90 cm laboratory cart with a 10 cm perimeter barrier) covered with absorbent paper. The rat was timed for 2 minutes, during which the activity level and gait characteristics were scored and ranked, and the number of grooms, rears, fecal boluses and urine pools were counted. A rear starts when both front feet leave the cart surface and ends when both front feet are returned to the cart surface. No distinction is made between supported and unsupported rearing. The rat is assigned an arousal score, a gait description and a gait score based upon its activities during the two minute exploratory period. At the end of 2 minutes, the rat was returned to the home cage and placed back in the animal room. The cart surface is disinfected with 10% Microquat solution and wiped with a paper towel. A new piece of absorbent paper is then placed upon the cart.

At 11 weeks, the rat underwent additional tests to assess elicited responses. At the end of the 2 minutes in the open arena the rat was scored on the response to the approach of a closed pen, response to a loud click, tail pinch response, pinna response and pupillary response to a pen light. Righting reflex was measured by placing the rat on its back on a padded surface. The rat was scored on how quickly it turned over onto its feet. To score aerial righting, the rat was held in the air at 20 centimeters with its back horizontal to a padded surface. The rat was released and scored on its ability to turn over to land on its feet. To measure hindlimb landing foot splay, the back feet of each rat was moistened

with water. The rat was held by the scruff of the neck and the base of the tail and dropped from 20 centimeters. The distance was measured from the center of the foot prints to the nearest 0.5 centimeter. This was repeated twice and the measures were averaged. Lastly, forelimb and hindlimb grip strength were measured with a Chantillon Digital Force Meter. To measure forelimb grip strength, the rat was held by the base of the tail. The rat was allowed to grip the grate of the meter and steadily pulled with consistent gentle force backwards until the grip was broken. To measure hindlimb grip strength, the rat was held by the base of the tail. The rat was allowed to grip the grate with its hindlimbs and then pulled back with steady consistent force until the hindlimb grip was broken. These measures were repeated 3 times and the measures were averaged.
To conclude the 11-week observations, the rat was then placed into a cage for motor activity monitoring. The cage was placed into the photobeam unit and testing lasted for 15 minutes. During this time, the number of beam breaks was recorded by the Flexfield software. Upon completion, the rat was returned to its homecage.

All data were recorded on standardized data sheets and later entered into Microsoft excel for data analysis.

Results

All analyses were performed separately for males and females.

For variables that were measured as a frequency of occurrence, a Chi-square analysis was used to compare the responses across all treatment groups followed by either a Chi-square analysis or a Fisher's exact test on pairs of treatment groups if the overall test was significant. Statistical significance was defined as $p<0.05$.

For variables that were continuous, the treatment groups and sexes were compared using a two factor analysis of variance (ANOVA) or a one factor ANOVA was used for each sex to compare the treatment groups. If the treatment groups were significantly different, then a Tukey's test was used to compare pairs of treatment groups.

SPSS 12.0 and 13.0 and Stat Xact were used to perform all analyses and statistical significance was defined as $p<0.05$ for all tests.

Week 11 observations

For total movement during motor activity monitoring, the males in the 12mg/kg RDX treatment group had a significantly higher total movement score then the 4 mg/kg RDX treatment group. Significant differences were also observed between males and females for foot splay and front limb grip strength. Males had a larger average foot splay than females. Males also had greater average front limb grip strength than females.

Open Arena Data

Discussion

Several of the open arena parameters were measured as normal or abnormal activity, with the abnormal activity having several possible descriptive answers. For ease of analysis and because many of those answers were not used, the answers were combined into two categories, normal and abnormal responses. Fecal description and gait description were combined into a normal and abnormal response. For fecal amount and piloerection, the responses were coded as normal or absent. For arousal, the answers were divided into three categories, slow to arouse, normal arousal, and high or quick to arouse.

Other parameters were counts of occurrences, number of grooms and number of rears; they were categorized prior to analysis. The number of grooms was so infrequent that these parameters were categorized as none, 1-5 and 6 or more. Number of rears had categories of 0, 1-5, 6-10, and 11 or more. The last 4 categories were made into one, 11 or more since there were very few responses in the 11-15, 16-20, and 20 or more categories.

Urination was originally scored as normal, anuria or a copious amount. There were very few copious amounts seen, so the urination parameter was recoded as normal or abnormal for the comparison of treatment groups.

There were significant treatment differences for males for fecal amount at week 11, urine amount at week 13, and rearing behavior at weeks 3 and 13 and number of grooms at week 11. For females there were significant treatment group differences for number of grooms at weeks 2, 9 and 12.

Home Cage Activity

Observations of posture changes and presence of agitation, tremors, and convulsions for each animal at each week were recorded. Comparisons of treatment groups at each week and for each sex were performed using a Chi square test. Very few significant treatment group differences were observed at the individual weeks for any parameter.

During week 6 only, there was a significant difference between treatment groups in the frequency of postures. The control group was in a sitting or standing posture significantly more often then the 4, 8 and 10 mg/kg RDX groups.

Hand Held Data

Hand held parameters, ease of removal, reaction to handling, lacrimation, salivation, unelicited pupil status and skin appearance, were analyzed at each week. The numbers (percents) of observations were compared across doses for males and females separately. Skin appearance was coded as normal or abnormal, plus types of abnormal appearance were tabulated and compared. Reaction to handling was coded as low (very low to moderately low) and high (moderately high to high). Ease of removal was coded as easy (very easy to easy) and difficult (moderate to difficult). A Chi-square analysis was used

to compare the frequency of the responses across all treatment groups followed by a Chi-square analysis or Fisher's exact test on pairs of treatment groups if the overall test was significant. Statistical significance was defined as $p<0.05$.

The females had significant differences for ease of removal at week 5, skin appearance at week 9 and 12 and barbering at weeks 9 and 12.

Conclusions

The data presented here does not reveal that there was a dose related effect on functional activity or neuromuscular behavior. Statistical significance was found in some observations (e.g. skin/fur appearance and barbering) versus control animals, however, this only occurred in the high dose females during weeks 9 and 12. Sporadic statistical significance, both between dose groups and versus control, was noted in many other parameters, but these findings were not believed to be compound related. In addition, no clear patterns or biological meanings could be derived from these findings.

Daily FOB screenings for this study could not begin until the dosing procedure was completed since the observer must be blinded to the dose group labels on the cage cards. Typically the dosing procedure was completed in approximately 2 hours. On many occasions, the co-investigators observed dosed animals with neurotoxic effects (e.g. convulsions) during the dosing procedure, but these effects had subsided by the time FOB screenings had been initiated. Although the observed neurotoxic effects were noted in the LABCAT observations, they were not recorded in the FOB observations. Therefore, it is the belief of the co-investigators, that the full neurotoxic potential of RDX dosed orally at 8 mg/kg/day and above was not observed in the FOB screening.

References

Moser, V.C. The Functional Observation Battery in Adult and Developing Rats. NeuroToxicology 2000; 21: 989-996

Statistical Analysis of the Functional Observation Battery (FOB) Test in Rats Administered RDX for 90 Days

Prepared by Robyn B. Lee

Revised December 21, 2005

Table of Contents

Abstract:

Male and female rats were randomly assigned to six RDX treatment groups (0, 4, 8, 10, 12, 15 mg/kg/day). Each dose was given orally, once a day, seven days a week for 90 days (13 weeks). The Functional Observation Battery (FOB) of tests was used to measure the effects of RDX. The FOB was conducted weekly and measurements were recorded for each animal with the observer being blinded to the treatment group. Measurements were made on hand held observations, open arena observations, motor activity and home cage observations. Statistical analyses were conducted separately for male and female animals using either Chi-square tests on categorical data or analysis of variance (ANOVA) on continuous type data. Comparison of treatment groups on the observations at each week was made. In general, there were very few statistically significant differences between sexes and treatment groups. The significant differences observed were mostly between the higher doses of RDX, 12 and 15 mg/kg/day, and the control and low doses 4 and 8 mg/kg/day.

Introduction:

Fifty male rats and 47 female rats were randomly assigned to six RDX treatment groups (Group #1 was the 0 mg/kg/day or control, #2 was the 4 mg/kg/day, #3 was the 8 mg/kg/day, #4 was the 10 mg/kg/day, # 5 was the 12 mg/kg/day and #6 was the 15 mg/kg/day.). Each dose was given orally, once a day, seven days a week for 90 days (13 weeks).

The Functional Observation Battery (FOB) of tests was one of the testing methods used in the 90 day study of the effects of RDX administered orally in rats. The FOB was conducted weekly and measurements were recorded for each animal with the observer being blinded to the treatment group. The statistical analysis was also conducted in a blinded fashion, not knowing the dosage of each treatment group. The FOB consisted of several types of observations, home cage activity, motor activity, hand held observations and open arena observations. These activities were used to compare the six dose groups to determine any dose effects.

Statistical Methods:

All analyses were performed separately for males and females.

For variables that were measured as a frequency of occurrence, a Chi-square analysis was used to compare the responses across all treatment groups followed by either a Chi-square analysis or a Fisher's exact test on pairs of treatment groups if the overall test was significant. Statistical significance was defined as $p<0.05$.

For variables that were continuous, the treatment groups and sexes were compared using a two factor analysis of variance (ANOVA) or a one factor ANOVA was used for each sex to compare the treatment groups. If the treatment groups were significantly different, then a Tukey's test was used to compare pairs of treatment groups.

SPSS 12.0 and 13.0 and Stat Xact were used to perform all analyses and statistical significance was defined as $p<0.05$ for all tests.

Week 11 Observations:

Week 11 observations included foot splay, front limb grip strength and hind limb grip strength. The treatment groups and sexes were compared using a two factor analysis of variance (ANOVA) followed by a Tukey's multiple comparison test to determine pairs of treatment differences. No significant treatments by sex interactions were observed. Significant differences between males and females were observed for foot splay and front limb grip strength, $p<0.05$. No significant treatment group differences were observed. Tables and graphs are displayed below for foot splay and front limb grip strength only.

Other observations made and analyzed were approach, auditory, pina, tail, surface and drop responses. These responses were categorical and treatment groups were compared using a Chi square test for each sex. No significant treatment group differences were observed for either sex for any of these response parameters; therefore, these data are not displayed in tables.

Table 1: Foot Splay

Average Foot Splay by Sex and Treatment Group

Foot Splay (mm)

sex		N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Min	Max
						Lower Bound	Upper Bound		
female	1	9	34.4	12.6	4.2	24.8	44.1	17.5	57.5
	2	9	44.4	4.1	1.4	41.3	47.6	37.5	50.0
	3	10	40.5	6.1	1.9	36.1	44.9	27.5	47.5
	4	8	36.9	7.3	2.6	30.8	43.0	27.5	47.5
	5	4	41.3	4.8	2.4	33.6	48.9	37.5	47.5
	6	6	40.0	7.7	3.2	31.9	48.1	27.5	50.0
Males*	1	10	56.0	18.8	6.0	42.5	69.5	30.0	100.0
	2	10	64.0	13.5	4.3	54.3	73.7	47.5	97.5
	3	9	56.7	6.6	2.2	51.6	61.8	45.0	62.5
	4	6	57.9	11.2	4.6	46.1	69.7	45.0	75.0
	5	8	59.4	16.1	5.7	45.9	72.8	40.0	90.0
	6	6	58.3	10.1	4.1	47.8	68.9	42.5	67.5

No significant treatment group differences observed.
*** Significant difference between sexes, males have larger average foot splays than females, $p<0.05$.**

Figure 1: Foot Splay by Treatment Group and Sex

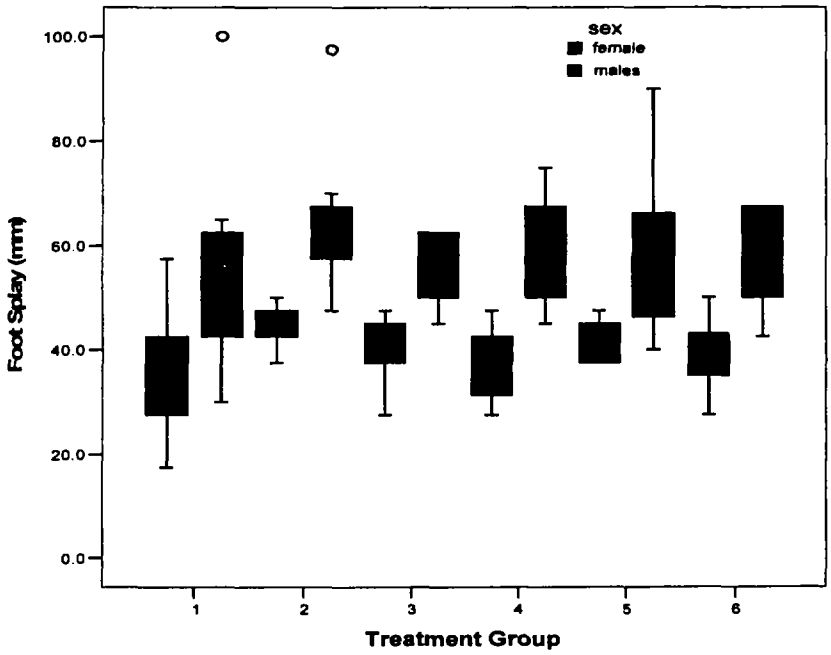


Table 2: Front Limb Grip Strength

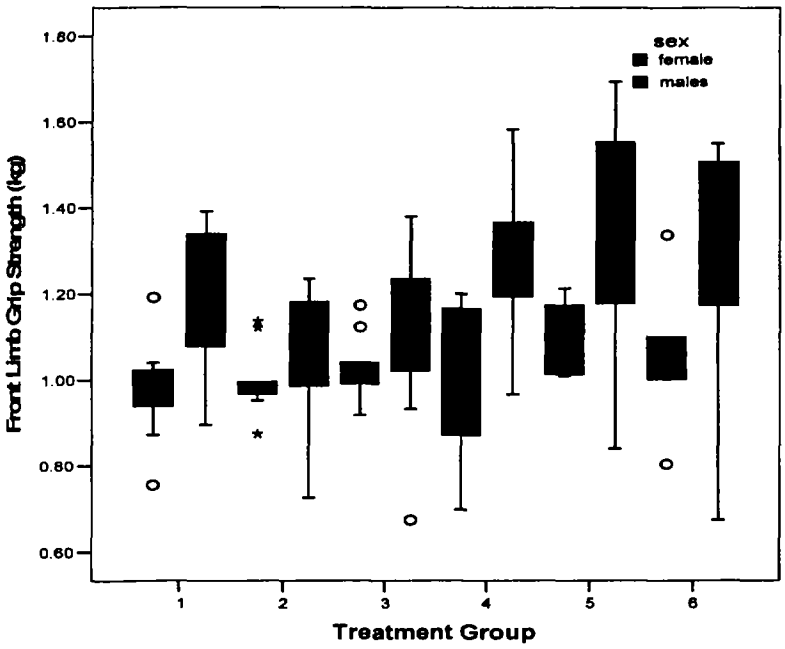
Average Front Limb Grip Strength by Sex and Treatment Group

Front Limb Grip Strength (kg)

sex		N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Min	Max
						Lower Bound	Upper Bound		
female	1	9	.97	.12	.04	.88	1.06	.76	1.19
	2	9	1.00	.08	.03	.93	1.06	.87	1.14
	3	10	1.02	.08	.02	.97	1.08	.92	1.17
	4	8	.98	.18	.06	.83	1.13	.70	1.20
	5	4	1.09	.10	.05	.94	1.25	1.01	1.21
	6	6	1.05	.17	.07	.87	1.23	.80	1.34
males*	1	10	1.18	.16	.05	1.07	1.29	.90	1.39
	2	10	1.04	.15	.05	.93	1.15	.73	1.24
	3	9	1.10	.21	.07	.94	1.27	.67	1.38
	4	6	1.28	.21	.08	1.07	1.50	.97	1.58
	5	8	1.35	.28	.10	1.11	1.59	.84	1.70
	6	6	1.24	.31	.13	.91	1.57	.67	1.55

*** Significant difference between sexes, males have greater average front limb grip strength than females, $p<0.05$.**
Borderline treatment group differences, $p=0.061$ for males (5>2,3), no significant treatment group differences for females.

Figure 2: Front Limb Grip Strength



Home Cage Activity:

Observations of posture changes and presence of agitation, tremors, and convulsions for each animal at each week were recorded. Comparisons of treatment groups at each week and for each sex were performed using a Chi square test. Very few significant treatment group differences were observed at the individual weeks for any parameter. Only the parameters and weeks that showed significant differences are displayed in the tables below.

No significant treatment group differences were observed for either sex for agitation, tremors or convulsions. No significant treatment group differences were observed for females for posture. For males at week 6 only, a significant difference between treatment groups in the frequency of postures was observed. Treatment groups 2, 3, and 4 were significantly different than treatment group 1, $p<0.05$.

Table 3: Posture Frequency

Males: Treatment Group by Postures Week 6

week				Posture		
				Lying Down	Sitting/standing	Rearing
6	Group	1	N	1	8	1
			%	10.0%	80.0%	10.0%
		2	N	3	2 *	5
			%	30.0%	20.0%	50.0%
		3	N	4	2 *	4
			%	40.0%	20.0%	40.0%
		4	N	5	2 *	2
			%	55.6%	22.2%	22.2%
		5	N	1	5	3
			%	11.1%	55.6%	33.3%
		6	N	0	7	3
			%	.0%	70.0%	30.0%

*** Significantly different than treatment group 1 with respect to the distribution of postures, $p<0.05$.**

Motor Activity:

An analysis of variance was used to compare the mean total movement between treatment groups for each sex, followed by a Tukey's test to test pairs of treatments for significant differences. No significant differences between treatment groups were observed for females. For males, A significant difference in total movement was observed between treatment group 2 and 5, $p<0.05$.

Table 4: Total Movement

Total Movement at Week 11 by Sex and Treatment Group

Total Movement

Sex		N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
						Lower Bound	Upper Bound		
female	1	10	392.1	75.2	23.8	338.3	445.9	223	483
	2	10	397.8	97.6	30.9	328.0	467.6	240	556
	3	9	461.2	138.6	46.2	354.7	567.8	210	607
	4	8	390.9	146.4	51.8	268.5	513.3	229	659
	5	5	421.6	108.1	48.3	287.4	555.8	351	613
	6	6	473.5	136.0	55.5	330.7	616.3	287	707
male	1	10	420.3	94.7	30.0	352.5	488.1	278	558
	2	10	375.1	66.4	21.0	327.6	422.6	257	468
	3	9	440.1	72.9	24.3	384.1	496.1	324	535
	4	8	379.9	110.8	39.2	287.3	472.5	267	531
	5	8	508.62 *	131.7	46.6	398.5	618.7	260	641
	6	8	390.3	76.8	27.1	326.1	454.4	237	489

*** For males, significantly different than treatment group 2, $p<0.05$.**

No significant differences between treatment groups observed for females.

Open Arena Data:

Several of the open arena parameters were measured as normal or abnormal activity, with the abnormal activity having several possible descriptive answers. For ease of analysis and because many of those answers were not used, the answers were combined into two categories, normal and abnormal responses. Fecal description and gait description were combined into a normal and abnormal response. For fecal amount and piloerection, the responses were coded as normal or absent. For arousal, the answers were divided into three categories, slow to arouse, normal arousal, and high or quick to arouse.

Other parameters were counts of occurrences, number of grooms and number of rears; they were categorized prior to analysis. The number of grooms was so infrequent that these parameters were categorized as none, 1-5 and 6 or more. Number of rears had categories of 0, 1-5, 6-10, and 11 or more. The last 4 categories were made into one, 11 or more since there were very few responses in the 11-15, 16-20, and 20 or more categories.

Urination was originally scored as normal, anuria or a copious amount. There were very few copious amounts seen, so the urination parameter was recoded as normal or abnormal for the comparison of treatment groups.

These data were analyzed to compare treatment groups for males and females separately, at each week. All measured/observed parameters were analyzed with a Chi-square test to determine overall treatment differences followed by a Fisher's exact test to compare pairs of treatment groups.

No significant treatment differences were observed for males or females for arousal, gait fecal description, and piloerection. No significant treatment differences were observed for females for urination, number of rears and fecal amount. Significant treatment differences were observed for males for fecal amount at week 11, urine amount at week 13, number of rears at weeks 3 and 13, and number of grooms at week 11. For females, significant treatment group differences were observed for number of grooms at weeks 2, 9 and 12.

Only the parameters which showed significant differences are displayed in the tables below.

Table 5a: Number of Grooms - Males

Males: Number of Grooms by Treatment Group Week 11

sex	week				# of Grooms		Total
					Zero	1-5	
Male	11	group	1	N	3	3	6
				%	50.0%	50.0%	100.0%
			2	N	0	7 *	7
				%	.0%	100.0%	100.0%
			3	N	4	2	6
				%	66.7%	33.3%	100.0%
			4	N	2	2	4
				%	50.0%	50.0%	100.0%
			5	N	0	4	4
				%	.0%	100.0%	100.0%
			6	N	3	1	4
				%	75.0%	25.0%	100.0%

*** Significantly different than treatment group 3 with respect to the frequency of the number of grooms, $p<0.05$.**

Table 5b: Number of Grooms - Females

Females: Number of Grooms by Treatment Groups Weeks

sex	week				# of Grooms			Total
					Zero	1-5	>=6	
Female	2	group	1	N	1	4	2	7
				%	14.3%	57.1%	28.6%	100.0%
			2	N	0	3 *	3	6
				%	.0%	50.0%	50.0%	100.0%
			3	N	0	6 *	0	6
				%	.0%	100.0%	.0%	100.0%
			4	N	1	6 *	1	8
				%	12.5%	75.0%	12.5%	100.0%
			5	N	0	6 *	0	6
				%	.0%	100.0%	.0%	100.0%
			6	N	5	2	0	7
				%	71.4%	28.6%	.0%	100.0%
	9	group	1	N	0	3	3 *, #	6
				%	.0%	50.0%	50.0%	100.0%
			2	N	0	4	3 *, #	7
				%	.0%	57.1%	42.9%	100.0%
			3	N	1	5	0	6
				%	16.7%	83.3%	.0%	100.0%
			4	N	3	5	0	8
				%	37.5%	62.5%	.0%	100.0%
			5	N	1	3	0	4
				%	25.0%	75.0%	.0%	100.0%
			6	N	3	2	0	5
				%	60.0%	40.0%	.0%	100.0%
	12	group	1	N	0	6 *, #, @	3	9
				%	.0%	66.7%	33.3%	100.0%
			2	N	0	10 *, #, @	0	10
				%	.0%	100.0%	.0%	100.0%
			3	N	2	7	0	9
				%	22.2%	77.8%	.0%	100.0%
			4	N	5	3	0	8
				%	62.5%	37.5%	.0%	100.0%
			5	N	3	1	0	4
				%	75.0%	25.0%	.0%	100.0%
			6	N	3	3	0	6
				%	50.0%	50.0%	.0%	100.0%

*** Significantly different than treatment group 6, p<0.05**
 # Significantly different than treatment group 4, p<0.05
@ Significantly different than treatment group 5, p<0.05

Table 6: Number of Rears

Males: Number of Rears by Treatment Group Weeks 3 and 13

sex	week				# of Rears				Total
					Zero	1-5	6-10	>=11	
Male	3	group	1	N	4	1	0		5
				%	80.0%	20.0%	.0%		100.0%
			2	N	1	4	0		5
				%	20.0%	80.0%	.0%		100.0%
			3	N	2	1	2		5
				%	40.0%	20.0%	40.0%		100.0%
			4	N	1	4	0		5
				%	20.0%	80.0%	.0%		100.0%
			5	N	2	3	0		5
				%	40.0%	60.0%	.0%		100.0%
			6	N	0	5 *	0		5
				%	.0%	100.0%	.0%		100.0%
	13	group	1	N	1	5	1	0	7
				%	14.3%	71.4%	14.3%	.0%	100.0%
			2	N	0	4	4	0	8
				%	.0%	50.0%	50.0%	.0%	100.0%
			3	N	0	3	4 *	0	7
				%	.0%	42.9%	57.1%	.0%	100.0%
			4	N	0	0	1	2 *	3
				%	.0%	.0%	33.3%	66.7%	100.0%
			5	N	0	2	4 *	0	6
				%	.0%	33.3%	66.7%	.0%	100.0%
			6	N	0	3	3 *	0	6
				%	.0%	50.0%	50.0%	.0%	100.0%

*** Significantly different than treatment group 1 with respect to the number of rears, p<0.05.**

Table 7: Fecal Amount

Males: Fecal Amount by Treatment Group Week 11

sex	week				Fecal Amount		Total
					Absent	Normal	
Male	11	group	1	N	4	2	6
				%	66.7%	33.3%	100.0%
			2	N	4	3	7
				%	57.1%	42.9%	100.0%
			3	N	6	0	6
				%	100.0%	.0%	100.0%
			4	N	0	4 *	4
				%	.0%	100.0%	100.0%
			5	N	1	3	4
				%	25.0%	75.0%	100.0%
			6	N	3	1	4
				%	75.0%	25.0%	100.0%

*** Significant difference between treatment groups 3 and 4 with respect to the frequency of normal fecal amounts observed, $p<0.05$.**

Table 8: Urine Amount

Males: Urine Amount by Treatment Group Week 13

sex	week				Urine Amount		Total
					Normal	Abnormal	
Male	13	group	1	N	1	6	7
				%	14.3%	85.7%	100.0%
			2	N	0	8	8
				%	.0%	100.0%	100.0%
			3	N	4	3	7
				%	57.1%	42.9%	100.0%
			4	N	3	0	3
				%	100.0%	.0%	100.0%
			5	N	6 *	0	6
				%	100.0%	.0%	100.0%
			6	N	2	4	6
				%	33.3%	66.7%	100.0%

*** Significantly different than treatment groups 1 and 2 for frequency of normal urine amounts, $p<0.05$.**

Hand Held Data:

Hand held parameters, ease of removal, reaction to handling, lacrimation, salivation, unelicited pupil status and skin appearance, were analyzed at each week. The numbers (percents) of observations were compared across doses for males and females separately. Skin appearance was coded as normal or abnormal, plus types of abnormal appearance were tabulated and compared. Reaction to handling was coded as low (very low to moderately low) and high (moderately high to high). Ease of removal was coded as easy (very easy to easy) and difficult (moderate to difficult). A Chi-square analysis was used to compare the frequency of the responses across all treatment groups followed by a Chi-square analysis or Fisher's exact test on pairs of treatment groups if the overall test was significant. Statistical significance was defined as $p<0.05$.

No significant treatment group differences were observed for males or females for reaction to handling, salivation, lacrimation and unelicited left or right pupil status. No significant treatment differences were observed for males for ease of removal, skin appearance or barbering. For females, significant treatment differences were observed for ease of removal at week 5, skin appearance at weeks 9 and 12 and barbering at weeks 9 and 12. Tables for the significant treatment differences are displayed below.

Table 9: Ease of Removal

Group * Reaction to Handling Crosstabulation

Sex	Week				Reaction to Handling		Total
					Low	High	
Female	12	Group	1	N	9	0	9
				%	100.0%	.0%	100.0%
			2	N	10	0	10
				%	100.0%	.0%	100.0%
			3	N	9	0	9
				%	100.0%	.0%	100.0%
			4	N	5	3	8
				%	62.5%	37.5%	100.0%
			5	N	4	0	4
				%	100.0%	.0%	100.0%
			6	N	5	1	6
				%	83.3%	16.7%	100.0%

*** Significantly different than treatment group 6, $p<0.05$.**

Table 10: Skin Appearance

Females: Skin Appearance by Treatment Groups Weeks 9 & 11

Sex	Week				Skin Appearance		Total
					Abnormal	Normal	
Female	9	Group	1	N	1	5	6
				%	16.7%	83.3%	100.0%
			2	N	1	6 *	7
				%	14.3%	85.7%	100.0%
			3	N	0	6 *	6
				%	.0%	100.0%	100.0%
			4	N	2	6	8
				%	25.0%	75.0%	100.0%
			5	N	0	4 *	4
				%	.0%	100.0%	100.0%
			6	N	4	1	5
				%	80.0%	20.0%	100.0%
	12	Group	1	N	0	9 *	9
				%	.0%	100.0%	100.0%
			2	N	0	10 *	10
				%	.0%	100.0%	100.0%
			3	N	2	7	9
				%	22.2%	77.8%	100.0%
			4	N	3	5	8
				%	37.5%	62.5%	100.0%
			5	N	0	4	4
				%	.0%	100.0%	100.0%
			6	N	3	3	6
				%	50.0%	50.0%	100.0%

*** Significantly different from treatment group 6, $p<0.05$.**

Table 11: Barbering

Females: Barbering by Treatment Groups Weeks 9 & 11

Sex	Week				Barbering		Total
					Present	Absent	
Female	9	Group	1	N	0	6 *	6
				%	.0%	100.0%	100.0%
			2	N	0	7 *	7
				%	.0%	100.0%	100.0%
			3	N	0	6 *	6
				%	.0%	100.0%	100.0%
			4	N	2	6	8
				%	25.0%	75.0%	100.0%
			5	N	0	4 *	4
				%	.0%	100.0%	100.0%
			6	N	4	1	5
				%	80.0%	20.0%	100.0%
	12	Group	1	N	0	9 *	9
				%	.0%	100.0%	100.0%
			2	N	0	10 *	10
				%	.0%	100.0%	100.0%
			3	N	2	7	9
				%	22.2%	77.8%	100.0%
			4	N	3	5	8
				%	37.5%	62.5%	100.0%
			5	N	0	4	4
				%	.0%	100.0%	100.0%
			6	N	3	3	6
				%	50.0%	50.0%	100.0%

*** Significantly different than treatment group 6, p<0.05.**

Compliance Statement

The statistical analysis of the FOB data for the RDX study in rats was conducted in compliance with Good Laboratory Practices (GLP).

Robyn B. Lee
Statistician

Aug 14, 2006
Date

APPENDIX W

IMMUNOTOXICITY ASSAYS

Table 1. Cellularity of spleen and thymus.

	Mean #cells x 10^3/µg organ mass ± SEM			
	Males		Females	
Treatment:	**Thymus**	**Spleen**	**Thymus**	**Spleen**
Control	1.01 ± 0.14	0.91 ± 0.19	1.28 ± 0.14	1.32 ± 0.19
4 mg/kg/d	0.72 ± 0.14	1.08 ± 0.19	1.04 ± 0.14	1.48 ± 0.19
8 mg/kg/d	0.87 ± 0.15	0.97 ± 0.20	1.16 ± 0.15	1.48 ± 0.20
10 mg/kg/d	0.69 ± 0.17	1.06 ± 0.23	1.11 ± 0.11	1.37 ± 0.21
12 mg/kg/d	0.73 ± 0.15	1.90 ± 0.27	0.83 ± 0.15	1.90 ± 0.27
15 mg/kg/d	0.82 ± 0.17	1.76 ± 0.25	1.49 ± 0.18	1.76 ± 0.25

Table 2. Expression of thymocyte antigens.

	Antigen expression (% positive)			
Treatment:	**CD4+8-**	**CD4+8+**	**CD4-8-**	**CD4-8+**
Males				
Control	3.8 ± 0.42	94.4 ± 1.06	1.1 ± 0.29	0.7 ± 0.08
4 mg/kg/d	4.0 ± 0.44	94.1 ± 1.11	1.3 ± 0.31	0.6 ± 0.09
8 mg/kg/d	4.0 ± 0.47	93.2 ± 1.18	1.9 ± 0.32	0.8 ± 0.09
10 mg/kg/d	3.4 ± 0.54	94.8 ± 1.37	1.2 ± 0.37	0.6 ± 0.11
12 mg/kg/d	3.5 ± 0.47	94.2 ± 1.18	1.6 ± 0.32	0.7 ± 0.09
15 mg/kg/d	4.4 ± 0.50	93.1 ± 1.26	1.9 ± 0.35	0.7 ± 0.10
Females				
Control	3.3 ± 0.42	92.8 ± 1.06	0.7 ± 0.29	0.6 ± 0.08
4 mg/kg/d	2.9 ± 0.42	95.7 ± 1.06	0.8 ± 0.29	0.6 ± 0.08
8 mg/kg/d	2.8 ± 0.44	95.9 ± 1.11	0.7 ± 0.31	0.6 ± 0.09
10mg/kg/d	3.6 ± 0.47	94.7 ± 1.18	1.1 ± 0.32	0.7 ± 0.09
12 mg/kg/d	2.7 ± 0.59	95.8 ± 1.50	0.9 ± 0.41	0.6 ± 0.12
15 mg/kg/d	2.7 ± 0.54	95.9 ± 1.37	0.9 ± 0.37	0.5 ± 0.11
P =				
Treatment	0.974	0.837	0.646	0.980
Sex	0.002†	0.098	0.001†	0.042
Interaction	0.498	0.322	0.622	0.377

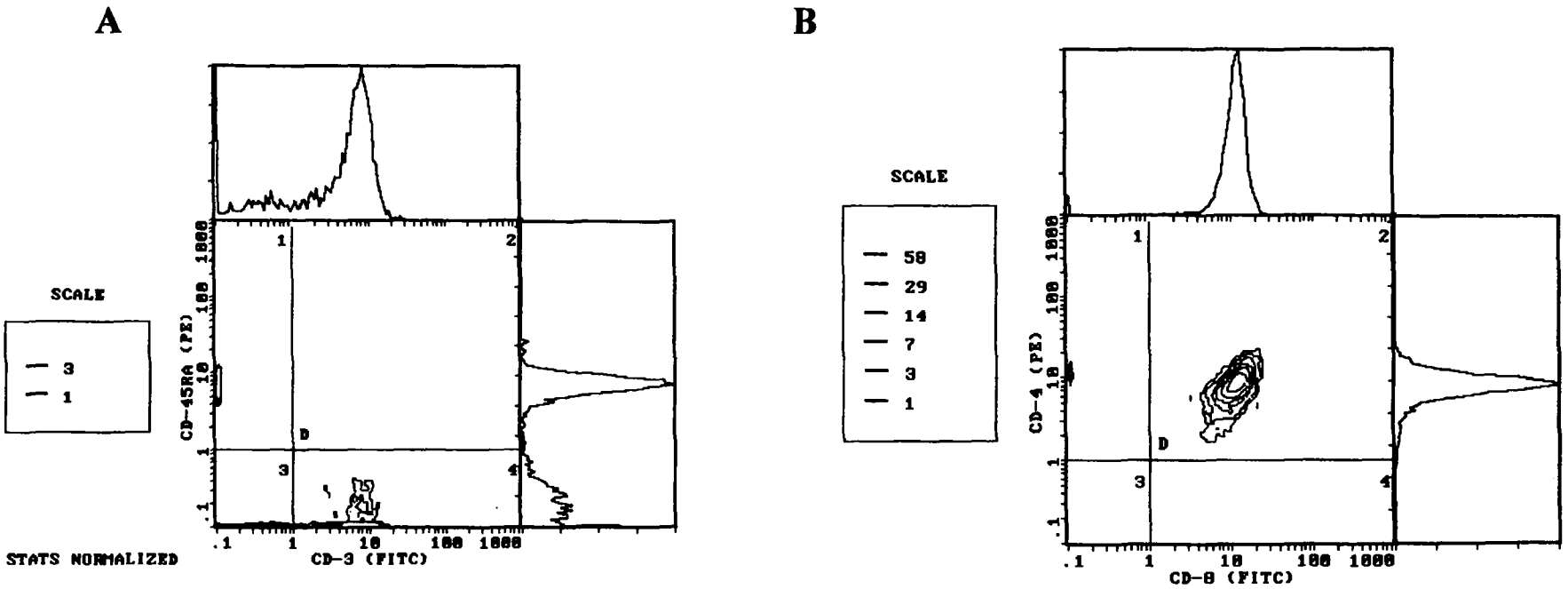
† Difference attributed to sex ($P < 0.05$).

Table 3. Expression of splenic antigens.

	Antigen expression (% positive)			
	Males		Females	
Treatment:	**CD3** (T-cell)	**CD45-RA** (B-cell)	**CD3** (T-cell)	**CD45-RA** (B-cell)
Control	36.0 ± 1.95	51.2 ± 2.42	36.0 ± 1.95	42.6 ± 2.30
4 mg/kg/d	31.8 ± 1.85	50.1 ± 2.30	36.0 ± 1.85	43.2 ± 2.20
8 mg/kg/d	33.1 ± 1.95	40.4 ± 2.42	36.4 ± 1.95	40.4 ± 2.42
10 mg/kg/d	34.7 ± 2.39	48.1 ± 2.97	36.0 ± 2.07	42.0 ± 2.57
12 mg/kg/d	32.4 ± 2.07	51.2 ± 2.57	35.4 ± 2.61	39.0 ± 3.25
15 mg/kg/d	30.3 ± 2.39	47.5 ± 2.75	39.0 ± 2.39	37.6 ± 2.97
P =				
Treatment	0.802	0.242		
Sex	0.004†	<0.001†		
Interaction	0.493	0.768		

† Difference attributed to sex ($P < 0.05$).

Fig. 1.
Representative scatter histograms of CD45-RA+ and CD3+ antigenic staining for the spleen (A) and CD4/CD8 staining for the thymus (B).



APPENDIX X

STUDY PROTOCOL AND MODIFICATIONS

US ARMY CENTER FOR HEALTH PROMOTION AND PREVENTIVE MEDICINE
PROTOCOL REVIEW, SUPPORT, APPROVAL SHEET

PROTOCOL NUMBER: 02-12-01

TITLE: Subchronic Oral Toxicity of RDX in Rats

A. PROTOCOL REVIEW:

1. Program Manager, TEP/HERP	Date	11/19/02	Approve/Disapprove
2. Scientific Merit	Date	11/19/02	Approve/Disapprove
3. Quality Assurance	Date	11/22/02	Approve/Disapprove

B. PROTOCOL SUPPORT:

4. Chief, Veterinary Medicine Division	Date	11/19/02	Support/Non-support
5. Chemistry	Date		Support/Non-support

C. PROTOCOL APPROVAL:

6. Chairman, IACUC	Date	13DEC02	Approve/Disapprove
7. Study Director	Date	18 MAR 03	Approve/Disapprove
8. Sponsor	Date		Approve/Disapprove

ANIMAL USE PROTOCOL
TOXICOLOGY DIRECTORATE
U.S. ARMY CENTER FOR HEALTH PROMOTION
AND PREVENTIVE MEDICINE
ABERDEEN PROVING GROUND, MD 21010-5403

PROTOCOL TITLE: Subchronic Oral Toxicity of RDX in Rats

PROTOCOL NUMBER: 5131-38-02-12-01

STUDY DIRECTOR:

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I. NON-TECHNICAL SYNOPSIS: The oral toxicity of RDX (1,3,5-trinitro-1,3,5-triazine), a commonly used military explosive, will be determined using a series of three laboratory studies in rats. The first study will be the acute approximate lethal dose (ALD), which will provide the lowest lethal dose of a single dose of the compound. Based upon the results of the ALD, a 14-day oral toxicity study will be performed in order to learn the effects and tolerance of repeated daily dosing with RDX. This study will serve as a range finding tool for the more definitive 90-day subchronic oral toxicity study. The 90-day study will yield data, which will permit the determination of a no observed adverse effect level (NOAEL), and therefore a reference dose, for RDX.

II. BACKGROUND

A. Background: This Center will support the combined efforts of the U.S. Army Corps of Engineers (COE) and the U.S. Army Environmental Center (AEC) (5179 Hoadley Road Aberdeen Proving Ground, MD 21010-5401) in attempting to change the Environmental Protection Agency (EPA) established reference dose for RDX. Cleanup goals for sites contaminated with explosive compounds and other contaminants are often established on the basis of risk assessments, which typically rely on the estimated oral toxicity of the substances of concern. These toxicity estimates are based on animal oral or feeding studies, which are capable of producing a reference dose derived from Lowest Observable Adverse Effect Level (LOAEL) and NOAEL values.

The current reference dose established for RDX was established using data from a chronic study performed on rats in 1983 (reference 1). However, several inadequacies were found when reviewing this study. First, the study

NOAEL was based on inflammation of the prostate. This is a common condition in older rodents and is generally not due to toxicity of the compound being administered, making it a poor endpoint on which to base a reference dose. Moreover, 85% of the animals that exhibited this condition were found dead or near death, making it likely that the animals simply had a bacterial infection. Second, the RDX administered to the rats was not pure, but was a military grade material that contained other explosive materials and impurities. Third, the RDX was administered to the rats indirectly in their feed rather than by directly by oral gavage. The proposed study will supersede the above mentioned chronic study because it will be done using pure RDX, administered via gavage, conducted using healthy animals, performed with six dosage groups rather than the previous four, and designed with closely spaced dosage groups to allow for a more accurate dose/response curve.

The study described will be conducted under Good Laboratory Practice (GLP) guidelines: 40 CFR (Code of Federal Regulations) 792, plus amendments (reference 2). The investigators and technicians will adhere to The Guide for Care and Use of Laboratory Animals (U.S. Department of Health, Education, and Welfare Publication No. NIH 86-23, 1996) (reference 3).

B. Literature Search:

1. Literature Source(s) Searched: A number of databases were consulted in an effort to obtain information on the subchronic toxicity of RDX. The databases were:

a. DTIC: Defense Technical Information Center
b. MEDLINE®: National Library of Medicine Database
c. TOMES Plus®
d. RTECS: Registry of Toxic Effects of Chemical Substances
e. HSDB: Hazardous Substance Data Bank
f. CHRIS: Chemical Hazard Response Information
g. Shepard's Catalog of Teratogenic Effects
h. TERIS: Teratogen Information System
i. REPROTOX: Reproductive Toxicology
j. IRIS: Integrated Risk Information System
k. New Jersey Hazardous Substance Fact Sheets
l. NIOSH Pocket Guide: National Institute for Safety and Health
m. North American Emergency Response Handbook
n. ECOTOX®: USEPA Environmental Databases
o. PHYTOTOX: Terrestrial Plant Database
p. TERRETOX: Terrestrial Animal Database
q. TOXLINE®
r. FED.RIP: Federal Reports In Progress
s. AGRICOLA: USDA National Agricultural Library
t. BRD: DoD Biomedical Research
u. CRISP: Computer Retrieval of Information on Scientific Projects

2. Date and Number of Search: August 26, 2002

3. Keywords of Search: RDX and Hexahydro-1,3,5-trinitro-1,3,5-triazine. When necessary, these search terms were linked with toxicity.

4. Results of Search: Findings relevant to this study are contained in the following section. Information from several of these studies were used as a reference to set the necessary dosage levels for the ALD.

a. The toxicity of RDX and TNT and their potential interactions in Fischer 344 rats were evaluated. Groups of 10 rats per sex received TNT in their diet at doses of 1, 5, 25, 125, or 300 mg/kg/day; RDX in their diet at doses of 10, 30, 100, 300, or 600 mg/kg/day; and the following combinations of these compounds; TNT 5/RDX 30 mg/kg/day, TNT 5/RDX 300 mg/kg/day, TNT 125/RDX 30 mg/kg/day, TNT 125/RDX 100 mg/kg/day, and TNT 125/RDX 300 mg/kg/day. Clinical signs, body weight, food consumption, hematology, clinical chemistry, organ

weights, and gross and tissue morphology was examined. Only the TNT results were reported in the citation (reference B.1.a).

b. The toxicity of RDX was evaluated in Fischer 344 rats when administered in the diet for up to 24 months. Groups of 75 rats/sex received RDX at doses of 0, 0.3, 1, 5, 8, 40 mg/kg/day. Interim kills were performed at 6 and 12 months (10 rats/sex/dose) with surviving animals sacrificed at 24 months. Toxicologic endpoints included clinical signs, body weights, food consumption, hematology, clinical chemistry, ophthalmology, organ weights, and gross and tissue morphology. Anemia with secondary splenic lesions, hepatoxicity, possible central nervous system involvement, cataracts, and urogenital lesions were observed in the rats sacrificed at 24 months. The no-effect level was set at 0.3 mg/kg/day based on the observance of increased levels of a hemosiderin-like pigment deposited in the spleen and suppurative inflammation of the prostate for rats administered with 1.5 mg/kg/day or greater (reference B.1.a).

c. The toxicity of TNT (.02, .1, and 1 mg/kg/day) and RDX (.1, 1, and 10 mg/kg/day) was tested in 42 rhesus monkeys. The munitions were given once a day, orally, seven days a week for 13 weeks. Five monkeys in the 10 mg/kg/day RDX dose group showed 12 instances of central nervous system disturbance, usually involving tonic convulsions. Histopathologic examination showed some increases in numbers of degenerate or necrotic megakaryocytes in bone marrow sections and increased amounts of iron-positive material in liver cord cytoplasm, both occurring in the high dosage groups of both RDX and TNT (reference B.1.a).

d. "The potential toxic interactions in Fischer 344 rats of the munition compounds trinitrotoluene (TNT) and hexahydro-1,3,5-trinitro-1,3,5-triazine (RDX) were examined following their coadministration in the diet. Groups of 10 rats per sex received TNT at doses of 5 or 125 mg/kg/day, RDX at doses of 30, 100, or 300 mg/kg/day, and combinations thereof for 13 weeks. Thirty rats per sex served as controls. Toxicologic endpoints included clinical observations, body weights, and tissue morphology. The major toxic effects following dietary administration of TNT to rats included anemia, hypercholesterolemia, and hepatomegaly, splenomegaly, and testicular atrophy with their accompanying histologic lesions. RDX intoxication in rats included hypotriglyceridemia, behavioral changes, and mortality. Most of the toxic effects of these chemicals were partially antagonized following their coadministration" (reference B.1.b).

e. The distribution and metabolism of RDX in the rat after subchronic administration was evaluated by dosing with either unlabeled RDX or [^{14}C]RDX by gavage at 20 mg/kg/day for 90 days or allowed free access to unlabeled RDX or [^{14}C]RDX-saturated drinking water (50-70 ug/ml) for up to 90 days. There was no RDX accumulation in any tissues nor were there any tendencies for plasma RDX to increase continuously with repeated dosing. The majority of the RDX was excreted as exhaled CO_2 and as unidentified metabolites in the urine. Eight of the thirty rats dosed with 20 mg/kg/day died due to exacerbation of chronic respiratory disease (reference B.1.b).

f. The oral toxicity of a RDX and TNT mixture typically found in munition plant effluents was evaluated in mice, rats, and dogs. Male and female rats were dosed with 574 and 594 mg/kg (single dose) and male and female mice were dosed with 947 and 1130 mg/kg (single dose). Dogs were repeatedly given 0.5, 5.0, or 50 mg/kg/day by capsule for up to 90 days. Rats were repeatedly given .005, .05, or .5% for 90 days while mice were repeatedly given .005, .05, .25, or .5% for 90 days. Mortality resulted at the highest dose level for each species. Observations for all three species included depressed body weight or body weight gain, depressed food intake, moderate to severe anemia, and alterations in the spleen, liver, and testes at the high dose levels. "Cholesterol was elevated in rats and dogs after 90 days. Uric acid values were elevated in rats but not in dogs, serum glutamic-pyrivic transaminase activity was low in dogs but unchanged in rats, and rats developed hypoplasia of the uterus but dogs did not. Signs of anemia were present at the intermediate dose levels. The lowest dose level in all three species was designated at a "no observable effects" level, based on the absence of clearly treatment-related effects (reference B.1.b).

g. TOMES reported that rats ingesting repeated doses of cyclonite at 25, 50, and 100 mg/kg displayed hyperirritability, convulsions, and mortality in 40%, 60%, and 87% of the animals, respectively. Lowest Observable Adverse Effect Levels (LOAELS) for oral rat exposures ranged from 1.5 to 160 mg/kg/day based on various effects including prostate inflammation, anemia, liver weight, central nervous system effects, mortality, body weight loss, and testicular degeneration. No Observable Adverse Effect Levels (NOAELS) for oral rat

exposures ranged from 0.3 to 80 mg/kg/day based on the same observations listed for the LOAELS (reference B.1.c).

h. Sixty male and sixty female rats were divided into groups of 10/sex and were fed diets that provided an RDX intake of 0, 10, 14, 20, 28, or 40 mg/kg/day for 13 weeks. Based on anemia, the LOAEL was 28 mg/kg/day and the NOAEL was 20 mg/kg/day (reference B.1.j).

i. Short-term toxicity studies were conducted with RDX in rats (strain and sex not specified). Groups of 15 rats received RDX in their diet at doses of 0, 15, 50, or 100 mg/kg/day for 10 weeks. The LOAEL was set at 50 mg/kg/day and the NOAEL at 15 mg/kg/day based on central nervous system effects. A follow-up study was conducted in 20 rats by the same route of administration at dosages of 0, 15, 25, or 50 mg/kg/day for 12 weeks. The LOAEL based on mortality and body weight loss was 25 mg/kg/day, and the NOAEL was 15 mg/kg/day (reference B.1.j).

j. "Male and female Sprague-Dawley rats were fed RDX at doses of 0, 1.0, 3.1, or 10 mg/kg/day for 24 months. Survival was comparable to controls in high-dose males and females. The LOAEL was 3.1 mg/kg/day and the NOAEL was 1 mg/kg/day based on decreased body weights in females" (reference B.1.j).

III. OBJECTIVE/HYPOTHESIS: The objective of these studies is to determine the relative oral toxicity of RDX in male and female rats. This information will, in turn, aid in the development of an accurate reference dose for the remediation of explosive contaminated land. It is hypothesized that ingestion of RDX will cause overt toxic signs in rats only at the higher dosage levels and that a NOAEL can be assigned to the munition compound upon completion of these studies.

IV. MILITARY RELEVANCE: RDX has been used extensively by the U.S. Military since the late 1930's. It has been reported to cause convulsions in military field personnel ingesting it and in munition workers inhaling its dust during manufacture. In addition, military bases across the United States have been contaminated due to the testing and disposal of RDX, and numerous other, military explosives (reference 4). It is possible that humans may be exposed to RDX during the remediation process and through contaminated groundwater used for human consumption. Current legislation (e.g. CERCLA, RCRA, NEPA, etc) requires a human health and ecological risk assessment of these contaminated sites before they can be cleaned up and transferred from military use. These risk assessments are typically based on references doses derived animal research that produces NOAEL and LOAEL values. In order to prevent inadvertent human health effects, accurate reference doses are essential.

V. MATERIALS AND METHODS:

A. Experimental Design and General Procedures:

1. **Procedure 1:** The detailed experimental design for the first range-finding study can be found in the Directorate of Toxicology Standard Operating Procedure (SOP) No. 17, "Approximate Lethal Dose (ALD) Procedure" (reference 5). The route of administration will be via gavage using pure RDX suspended in corn oil injected through a 16 GA x 2 inch gavage needle. Pure RDX will be procured from Umatilla Army Depot, Hermistion, Oregon. Chemical analysis will be performed by the USACHPPM Directorate of Laboratory Science (DLS) as needed in this and subsequent studies in order to meet Good Laboratory Practice Standards. This study will require eight young adult rats of each sex in order to properly assess the acute oral lethality of RDX. One rat of each sex will be assigned to each of the following dosage groups: 20, 30, 45, 68, 101, 152, 228, and 342 mg/kg. In order to comply with the body weight requirements set forth in the SOP as well as the U.S. Environmental Protection Agency (EPA) test guidelines, ten rats of each sex will be ordered. Extra rats will be used for quality assurance at the direction of the attending veterinarian.

2. **Procedure 2:** In order to determine the effect of repeated oral exposure to RDX, a 14-day oral toxicity study in rats will follow, with dosage levels based upon the results of the ALD. The detailed experimental design for this study can be found in SOP No. 37, "14-Day Range Finding and 90-Day Feeding Studies in Rats" (reference 6). As in the ALD, the route of administration will be via gavage using pure RDX suspended in corn oil injected through a 16 GA x 2 inch gavage needle. Forty-eight rats of each sex will be distributed into eight groups of six male and six female rats per group. Seven dosages are to be set at 2x, 1x, 0.5x, 0.25x, 0.125x, 0.0625x, and

0.03125x where x is the ALD value. One additional group shall serve as a corn oil control. The range of dosages listed above has historically produced usable results for the 90-Day study dosage selection. The number of animals to be used is the minimum needed for meaningful statistical evaluation. Two extra rats of each sex will be ordered for quality assurance.

3. Procedure 3: The main element will be the 90-day subchronic oral toxicity study. Again, the detailed experimental design for this study can be found in SOP No. 37, "14-Day Range Finding and 90-Day Feeding Studies in Rats." Since the report generated by the conduct of this study must be EPA-submittable, this procedure shall closely adhere to the EPA Health Effects Testing Guidelines [40CFR, Part 798.2650]. Where the SOP and the CFR differ, the SOP will take precedence. The route of administration will be by gavage with pure test compound suspended in corn oil injected through a 16 GA x 2 inch gavage needle five days a week for a period of 90-days. Seventy rats of each sex will be distributed into six dosage groups and a corn oil control group, the minimum number of animals required by the EPA to replace the existing study used to establish the reference dose. Eight extra rats of each sex will be ordered for quality assurance.

In addition, one-half of each spleen and thymus from five animals of each sex in each treatment group will be used to assess immunotoxicity in the rats. The assays included in this study are: 1) cellularity of a primary lymphoid organ (thymus) and a secondary lymphoid organ (spleen), and 2) quantification of lymphocyte sub-populations using cell surface marker identification. A detailed explanation of the immunotoxicity procedures can be found in SOP No. 128, "Assessing Immunotoxicity in Rats: Adapting Methods Amenable to a Sub-Chronic Study."

B. Laboratory Animals Required and Justification:

1. **Non-Animal Alternatives Considered:** No tissue culture, cell culture, or computer modeling procedure would produce the data needed to support an EPA submittable toxicological evaluation. A live, intact mammalian model with its biological complexity will be required to yield a NOAEL which can be extrapolated to human exposure to RDX.

2. **Animal Model and Species Justification:** The EPA Health Effects Test Guidelines state that a mammalian species shall be used and that the rat is the preferred species.

3. **Laboratory Animals**

   a. **Genus and Species:** Rattus norvegicus

   b. **Strain/Stock:** Sprague-Dawley

   c. **Source/Vendor:** Charles River Laboratories Wilmington, MA (USDA 14-R-0144)

   d. **Age:** 4-6 weeks (depending on availability)

   e. **Weight:** Approximately 200-300 grams at study start for males and 150-250 grams for females

   f. **Sex:** Male and Female

   g. **Special Considerations:** Vendor will provide health status upon delivery

   h. **Other:** N/A

4. **Total Number of Animals Required and Rationale:** 276 total (126 males and 126 females (plus 12 extra rats of each sex for quality assurance). The number of dose groups and animals/dose group were required by the EPA to supercede the existing study used to establish the reference dose.

5. **Refinement, Reduction, Replacement:**

a. **Refinement:** The LABCAT® data management system will be used to record body weights, food weights, and test system observations. This refinement will allow for a precise and complete record of the in-life portions of the 14- and 90-day studies. Animals will be handled daily by either the animal caretakers or the investigators for enrichment.

b. **Reduction:** The number of animals employed is the minimum possible required by the EPA to replace the existing study used to establish the reference dose for RDX.

c. **Replacement:** There is no acceptable methodology available to replace these studies.

C. Technical Methods:

1. **Pain:** Pain or distress can be anticipated in the higher dosage levels of the ALD and the 14-day oral studies. This will be due to the fact that the studies are range-finders which are designed to ascertain the maximum tolerable dosages of RDX, both acutely and repeatedly. Some pain will be associated with the 90-day study in the highest dosage level since, according to testing guidelines, toxic effects must be produced. The gavage procedure would not be considered distressful.

a. **USDA Pain Category:**

(1) **No Pain** 24 (8%) (Column C)

(2) **Alleviated Pain** 176 (64%) (Column D)

(3) **Unalleviated Pain or Distress** 76 (28%) (Column E)

b. **Pain Alleviation:** Alleviation of pain will not be indicated for these studies as signs of toxicity could be masked. These signs will be critical to the meaningful interpretation of each study. Animals in the alleviated pain category are not expected to experience pain or distress from the RDX exposure, however, they will be anesthetized for terminal blood sampling via cardiac puncture which is considered to be a painful procedure.

(1) **Anesthesia/Analgesia/Tranquilization:** Combination of xylazine/ketamine for terminal blood sampling only (10 mg/kg xylazine plus 90 mg/kg ketamine intra-muscular via a 22 gauge or smaller needle).

(2) **Paralytics:** None

c. **Alternatives to Painful Procedures:**

(1) **Source(s) Searched:** DTIC: Defense Technical Information Center
MEDLINE®: National Library of Medicine Database
TOMES Plus®
RTECS: Registry of Toxic Effects of Chemical Substances
HSDB: Hazardous Substance Data Bank
CHRIS: Chemical Hazard Response Information
Shepard's Catalog of Teratogenic Effects
TERIS: Teratogen Information System
REPROTOX: Reproductive Toxicology
IRIS: Integrated Risk Information System
New Jersey Hazardous Substance Fact Sheets
NIOSH Pocket Guide: National Institute for Safety and Health
North American Emergency Response Handbook
ECOTOX®: USEPA Environmental Databases
PHYTOTOX: Terrestrial Plant Database
TERRETOX: Terrestrial Animal Database
TOXLINE®

FED.RIP: Federal Reports In Progress
AGRICOLA: USDA National Agricultural Library
BRD: DoD Biomedical Research
CRISP: Computer Retrieval of Information on Scientific Projects

(2) **Date of Search:** August 26, 2002

(3) **Key Words of Search:** RDX, oral, toxicity, feeding study, NOAEL, subchronic

(4) **Results of Search:** The results of the search indicate that several similar studies have been performed on RDX, however, they did not provide adequate information for the establishment of an accurate reference dose. All of the previously described studies were performed in laboratory animals, with no indication of non-animal alternatives.

d. **Painful Procedure Justification:** The nature of the studies precludes the use of totally painless procedures. However, to prevent undue suffering, rats that appear moribund will be evaluated by the principal investigator and the Attending Veterinarian and may be euthanized as described in section V.7. If it is determined that the animal needs to be euthanized, it will be anesthetized for terminal blood sampling and then submitted for necropsy. One or more of the following clinical signs will be indicative of a moribund animal: impaired ambulation, which prevents animals from reaching food or water; excessive weight loss and extreme emaciation ($\geq$ 20% body weight); lack of physical or mental alertness; difficult labored breathing; and a prolonged inability to remain upright. The Attending Veterinarian will be consulted when necessary to evaluate moribund animals.

2. **Prolonged Restraint:** Not applicable

3. **Surgery:** Not applicable

a. **Procedure:** Not applicable

b. **Pre- and Post-Operative Provisions:** Not applicable

c. **Location:** Not applicable

d. **Multiple Survival Surgery Procedures:** Not applicable

(1) **Procedures:** Not applicable

(2) **Scientific Justification:** Not applicable

4. **Animal Manipulations:**

a. **Injection:** As described in V.C.1.b.(1)

b. **Biosamples:** Approximately 5-7 ml of blood will be drawn from each rat just prior to necropsy in procedures 2 and 3. Each animal will be anesthetized using xylazine/ketamine and a cardiac blood sample taken as per SOP No. 53 "Animal Bleeding Techniques" (reference 8). Following sampling, each rat will be euthanized using CO_2 inhalation and submitted immediately thereafter for necropsy.

c. **Animal Identification:** Individual animals will be identified by implantable microchip and cage card according to SOP No. 03 "Individual Animal Identification" (reference 9).

d. **Behavioral Studies:** Not applicable

e. **Other Procedures:** Daily oral gavaging, as described in section V.

5. **Adjuvants:** None

6. **Study Endpoint:** All three of these procedures will have specific endpoints as defined by the Directorate SOPs. By definition, euthanasia will be the endpoint of the ALD. Euthanasia will also be the ultimate endpoint of the 14- and 90-day studies since blood must be drawn and tissues must be examined. No NOAEL can be determined without these observations.

7. **Euthanasia:** Euthanasia will be performed via CO_2 after anesthesia for blood sample collection by the co-investigators as specified by SOP No. 66 "Animal Euthanasia" and in accordance with AVMA guidelines (reference 10).

D. Veterinary Care:

1. Husbandry Considerations:

a. Study Room: Studies will be conducted at the USACHPPM Toxicology Directorate facilities, Bldg E-2100, Aberdeen Proving Ground, MD 21010-5403. The animal facilities are fully accredited by The Association for the Assessment and Accreditation of Laboratory Animal Care (AAALAC).

b. Special Husbandry Provisions: None

2. Attending Veterinary Care: All animals will be observed and handled on a daily basis by the animal caretakers and a member of the study staff to assess their health and welfare. Observations will be more frequent if needed to promptly identify animals that should be euthanized to prevent unnecessary pain and distress. Appropriate methods of animal care shall be maintained to prevent, control, diagnose and treat diseases and injuries. Animal users are trained in the handling, immobilization, anesthesia, analgesia and euthanasia of the laboratory rat. If an animal becomes ill or injured, the observer will report to the attending veterinarian. The animal will be euthanized by the animal care staff if it becomes critically ill or comatose. Supportive care will be provided by the animal care staff for clinically ill animals if euthanasia is delayed (other than illness associated with the administration of the test compounds).

3. Enrichment Strategy: Animal caretakers and principle investigators will handle rats daily prior to the dosing regimen to acclimate them to the study. Animals will also be handled daily as part of the dosing procedure.

a. Dogs: Not applicable

b. Nonhuman Primates: Not applicable

E. Data Analysis: Food consumption, body weights, organ-to-brain weight ratios and organ-to-by weight ratios will be compared among dosage groups and controls using a one-way analysis of variance (ANOVA) and, if statistical significance is found, Dunnett's post hoc test will be used to compare dosage groups to the control group. Those parameters will be collected within the LABCAT system and statistically analyzed using Sigma-Stat (Sigma-Stat, Jandel Scientific, Corte Madera, CA). Clinical chemistry, hematology, and urinalysis data will be entered into Sigma-Stat using a one- way ANOVA and Bonferroni's post hoc test to compare dosage groups to the control group. Where a normality test has failed after the data has been log transformed, an ANOVA on ranks will be performed. Immunotoxicity results will be statistically compared to controls using a one-way ANOVA and, when significance is observed, the data will be further analyzed using a Tukey test. Statistical significance will be defined at $p<.05$ level..

F. Investigator & Technician Qualifications/Training: All investigators named in this study have demonstrated an understanding of the humane care and use of research animals. They have taken part in discussions of pertinent laws and regulations concerning the use of animals in biomedical research in the Department of Defense as required by Public Laws 89-544, 91-579, and 99-198 (The Animal Welfare Act and Amendments, DOD Directives, and Army Regulations). They are familiar with the concepts for the reduction or elimination of the use of animals and have concluded that there is a need for the use of animals in this study. They have been familiarized in the proper methods for minimizing and/or alleviating pain in the animal species selected for study. They will either have an animal technician assigned to assist them who is an expert in the animal techniques required for the

study, or have exhibited sufficient proficiency themselves to justify allowing them to work unassisted or without the direct guidance from the laboratory veterinary staff. They have been advised on the animal care and use policy at this institution and are aware of the established reporting mechanisms for the observed deficiencies in animal care and treatment. Appendix A contains a list of personnel supporting this protocol.

VI. Biohazard/Safety: Normal adherence to standard chemical and animal handling procedures will be required during the performance of these studies. RDX will be considered a potentially hazardous material and handled in accordance with SOP No. 83 "Health and Safety of Laboratory Personnel" (reference 11).

VII. ASSURANCES: As the Principal Investigator on this protocol, I provide the following assurances:

A. Animal Use: The animals for use in this protocol will be used only in the activities and in the manner described herein, unless a deviation is specifically approved by the IACUC.

B. Duplication of Effort: I have made a reasonable, good faith effort to ensure that this protocol is not an unnecessary duplication of previous experiments.

C. Statistical Assurance: I assure that I have consulted with an individual who is qualified to evaluate the statistical design or strategy of this proposal, and that the minimum number of animals determined by EPA guidelines will be used.

D. Biohazard/Safety: I have taken into consideration, and I have made the proper coordinations regarding all applicable rules and regulations regarding radiation protection, biosafety, recombinant issues, etc., in the preparation of this protocol.

E. Training: I verify that the personnel performing the animal procedures/manipulations described in this protocol are technically competent and have been properly trained to ensure that no unnecessary pain or distress will be caused as a result of the procedures/manipulations.

F. Responsibility: I acknowledge the inherent moral and administrative obligations associated with the performance of this animal use protocol, and I assure that all individuals associated with this project will demonstrate a concern for the health, comfort, welfare, and well-being of the research animals. Additionally, I pledge to conduct this study in the spirit of the fourth "R" which the DOD has embraced, namely, "Responsibility" for implementing animal use alternatives where feasible, and conducting humane and lawful research.

Michael A Mayer
(S.D. Signature)

G. Painful Procedures: I am conducting biomedical experiments, which may potentially cause more than momentary or slight pain or distress to animals that WILL/WILL NOT (circle one) be relieved with the use of anesthetics, analgesics and/or tranquilizers.

Michael A Mayer
(S.D. Signature)

VIII. Study Time Frame:

A. Estimated Start Date: October 2002

B. Estimated Completion Date: April 2003

C. Archiving: Day to day records will be maintained in an official USACHPPM Notebook(s) in Building E2100 and eventually in the Toxicity Evaluation Program Archives in Building E2100.

IX. Enclosures:

A. Support Personnel

B. References

C. SOP's

APPENDIX A

SUPPORT PERSONNEL

1. **Veterinary Medicine Division:**

MAJ Goodwin, D.V.M.	Attending Veterinarian
Terry Hanna	Animal Caretaker
Robert Sunderland	Animal Caretaker
Richard Arnold	Animal Caretaker

2. **Toxicity Evaluation Program:**

Lee Crouse	Biologist, Co-Investigator
Mark Michie	Biologist, Co-Investigator
Hubert Snodgrass	Biologist
John Houpt	Biologist
Patricia Beall	Biologist
Jeff Bergmann	Biologist
Heidi Ilg	Biologist
Matthew Bazar	Biologist

3. **Heath Effects Research Program:**

Dr. Michael Major	Program Manager, HERP
Dr. Mark Johnson	Toxicologist
Dr. Karen Walker	Toxicologist

3. **Chemistry :**

Michael Hable	DLS Analytical Chemist

4. **Strategic Initiatives Office:**

Gene Sinar	Quality Assurance Assessor
Mike Kefauver	Quality Assurance Assessor

APPENDIX B

REFERENCES

1. United States Environmental Protection Agency, Integrated Risk Information System. September 1988. RDX. Internet, Accessed August 26, 2002.

2. Title 40, Code of Federal Regulations (CFR), Part 792, Good Laboratory Practice Standards.

3. Guide for the Care and Use of Laboratory Animals, U.S. Department of Health, Education, and Welfare, Publication No. NIH86-23, 1996.

4. HSDB: Hazardous Substance Data Bank. National Library of Medicine, Bethesda, MD, Internet, MICROMEDEX, Englewood, CO, Edition expires 2002.

5. Directorate of Toxicology, Standard Operating Procedure (DTOX SOP) 17.02. Approximate Lethal Dose (ALD) Procedure. USACHPPM, Aberdeen Proving Ground, MD.

6. Directorate of Toxicology, Standard Operating Procedure (DTOX SOP) 37.02. 14-Day Range Finding and 90-Day Feeding Studies in Rats. USACHPPM, Aberdeen Proving Ground, MD.

7. Directorate of Toxicology, Standard Operating Procedure (DTOX SOP) 128.02. Assessing Immunotoxicity in Rats: Adapting Methods Amenable to a Sub-Chronic Study. USACHPPM, Aberdeen Proving Ground, MD.

8. Directorate of Toxicology, Standard Operating Procedure (DTOX SOP) 53.02. Animal Bleeding Techniques. USACHPPM, Aberdeen Proving Ground, MD.

9. Directorate of Toxicology, Standard Operating Procedure (DTOX SOP) 03.02. Individual Animal Identification. USACHPPM, Aberdeen Proving Ground, MD.

10. Directorate of Toxicology, Standard Operating Procedure (DTOX SOP) 66.02. Animal Euthanasia. USACHPPM, Aberdeen Proving Ground, MD.

11. Directorate of Toxicology, Standard Operating Procedure (DTOX SOP) 83.02. Health and Safety of Laboratory Personnel. USACHPPM, Aberdeen Proving Ground, MD.

TOXICOLOGY PROGRAM
PROTOCOL MODIFICATION

Date of Modification: 20 November 2002

Protocol Title: Subchronic Oral Toxicity of RDX in Rats

Study Director: Dr. Michael Major

MODIFICATION

Pg. para. section

1, V.C.1.d. Modification: For the ALD portion of the study only, change "moribund rats will be anesthetized...and will then be euthanized" to "Animals showing signs of being moribund will be put on a more frequent observation schedule

Modification Con't
~~Reason:~~ and further evaluated to determine if euthanasia is necessary. The 14- and 90-day portions of the study will be handled as originally stated in the protocol.

2, Reason:
~~Modification:~~ By definition, an ALD is the lowest dose which is lethal where two successively higher doses are lethal and three doses lower are not lethal. However, animals showing toxic signs may recover. If the animals

Reason(Con't) are euthanized prematurely, a lethal dose will not be determined leading to inaccurate dosage levels for the 14-day study. By using an ALD instead of an LD50, every effort has been made to minimize the number of

3, Reason (Con't)
~~Modification:~~ animals used. The EPA was consulted on this issue, and they agree that animals on acute studies should be given the chance to recover, rather than euthanized immediately.

Reason:

4, Modification:

Reason:

Study Director — Date: 20 NOV 02

Principal Investigator — Date: 20 Nov 02

Chairman, IUC — Date: 13DEC02

DISTR: Study File, QAU, Archives, Sponsor

CHPPM Form 28-E, 1 May 1996 (MCHB-DL-TE)

TOXICOLOGY PROGRAM
PROTOCOL MODIFICATION

Date of Modification: 19 March 03

Protocol Title: Subchronic Oral Toxicity of RDX in Rats

Study Director: Dr. Michael Major

MODIFICATION

Pg. para. section

1, Pg.4 V.A.1. Modification: The dose groups for the female ALD rats will be changed to 13.35, 20, 30, 45, 68, 101, 152, ~~and~~ 228 mg/kg. and 342

Reason: It was discovered after dosing the male ALD rats that the dosages were set too high, so the groups were lowered by one factor to achieve more accurate results in the females.

2, _____ Modification:

Reason:

3, _____ Modification:

Reason:

4, _____ Modification:

Reason:

Michael Major 19MAR03
Study Director Date

Principal Investigator 19 March 03
Date

~~Chairman, AUC~~ Date

DISTR: Study File, QAU, Archives, Sponsor

CHPPM Form 28-E, 1 May 1996 (MCHB-DL-TE)

TOXICOLOGY PROGRAM
PROTOCOL MODIFICATION

Date of Modification: August 6, 2003

Protocol Title: Subchronic Oral Toxicity of RDX in Rats

Study Director: Dr. Michael Major

MODIFICATION

Pg. para. section

1, V.C.1.b.(1) Modification: Rats will be anesthetized using CO2 for a brief period of time prior to terminal blood sampling rather than the cocktail of xylazine/ketamine described in the original protocol.

Reason: It was discovered during previous terminal blood sampling that the ketamine/xylazine mixture slows the rats circulation to the point that blood sampling is very difficult. Valuable data is lost if blood samples cant be taken.

2, _____ Modification:

Reason:

3, _____ Modification:

Reason:

4, _____ Modification:

Reason:

_____ _____
Study Director Date

_____ 8/6/03
Principal Investigator Date

_____ 8AUG-03
Chairman, AUC Date

DISTR: Study File, QAU, Archives, Sponsor

CHPPM Form 28-E, 1 May 1996 (MCHB-DL-TE)

TOXICOLOGY PROGRAM
PROTOCOL MODIFICATION

Date of Modification: 8/5/04

Protocol Title: Subchronic Oral Toxicity of RDX in Rats

Study Director: Dr. Michael Major

MODIFICATION

Pg. para. section

1, All Sections — Modification:

The entire study, including the ALD, 14-day, and subchronic portions, must be repeated with the changes listed below.

Reason: Due to APG safety regulations, the dosing solution containing RDX had to be mixed by an explosive certified lab at RDECOM. Since the corn oil/RDX suspension was only stable for two weeks, fresh dosing solution was mixed

2, _____ Reason con't Modification:

every two weeks. Each batch of dosing solution was analyzed to determine if it was the proper concentration. It was discovered 6 weeks into the study that the dosing solution concentrations were both inconsistent and

Reason: con't

inaccurate. Since we were almost halfway into the study, it was decided to continue with the study and see if the concentrations improved. The concentrations did not improve and varied more than 20%. Since the

3, _____ Reason con't Modification:

dosing solution concentrations were both inaccurate and inconsistent, the results could not be used for EPA submission.

Reason:

4, II, B, 2 — Modification:

The literature search was updated in July 2004 with no new additions to make.

Reason:

The previous literature search was out of date.

Michael A Major 6AUG04 — Study Director — Date

[signature] 8/6/04 — Principal Investigator — Date

[signature] 6AUG04 — Chairman, AUC — Date

DISTR: Study File, QAU, Archives, Sponsor

CHPPM Form 28-E, 1 May 1996 (MCHB-DL-TE)

TOXICOLOGY PROGRAM
PROTOCOL MODIFICATION

Date of Modification: 8/5/04

Protocol Title: Subchronic Oral Toxicity of RDX in Rats

Study Director: Dr. Michael Major

MODIFICATION

Pg. para. section		
1, II, V, A, 1,2,3	Modification:	The RDX will be suspended in a mixture of distilled water, 1% methylcellulose, 0.2% Tween 80 instead of corn oil
	Reason:	Due to the nutritional value of corn oil, the EPA requested that a diluent be used that will not affect food consumption. The above mentioned mixture is commonly used as a diluent and is not toxic.
2, II, V, A, 2,3	Modification:	Animals will be dosed seven days a week for the 14-day and 90-day phases of the study.
	Reason:	The study is attempting to replace a two year study performed in 1983. In order to replace the longer study with a subchronic study, the rats must be dosed seven days a week.
3, V, B, 3, b,e	Modification:	The rat strain/stock will be changed to Fischer 344 and the weight will become 50-125 grams at study initiation.
	Reason:	The EPA has stated that inbred rats, such as Fischers, are not as susceptible to prostate inflammation as the outbred rats used in the previous study.
4, V, B, 4	Modification:	The total number of animals required will change from 276 to 281.
	Reason:	The immunotoxicity assessment requires the use of 5 spleens for calibration purposes. The rats must be separate from those on study because they will be euthanized several days prior to the end of the in-life portion of the ~~study~~.

Michael A Major 6 AUG 04
Study Director Date

Principal Investigator 8/6/04
Date

Chairman, IUC 6 AUG 04
Date

DISTR: Study File, QAU, Archives, Sponsor

CHPPM Form 28-E, 1 May 1996 (MCHB-DL-TE)

TOXICOLOGY PROGRAM
PROTOCOL MODIFICATION

Date of Modification: 8/5/04

Protocol Title: Subchronic Oral Toxicity of RDX in Rats

Study Director: Dr. Michael Major

MODIFICATION

	Pg. para. section		
1,	V, C, 1, a	Modification:	The USDA pain categories will change to the following due to the addition of 5 rats. No pain = 29 (10%) Alleviated Pain = 176 (63%) Unalleviated Pain = 76 (27%)
		Reason:	The addition of five animals changed the pain category percentages.
2,	Mod. (8/6/03)	Modification:	Rats will be anesthetized with a cocktail of ketamine/acetylpromazine rather than CO2 for terminal blood sampling.
		Reason:	Recent blood sampling for other studies have indicated that the ketamine/acetylpromazine cocktail is more effective than CO2 for blood sampling and also appears to be more humane for the animals.
3,	IACUC Recomm.	Modification:	The IACUC Committee required that written documentation must be obtained from the EPA stating that the results from the original RDX study were not submittable and why prior to ordering rats for the second study.
		Reason:	As per LTC Boles conversation with Dr. Knapik, the animals can be ordered prior to receiving the EPA documentation assuming that the documentation will be received as soon as possible.
4,		Modification:	
		Reason:	

Michael A Major 6 AUG 04
Study Director Date

Principal Investigator 8/6/04
Date

Joseph Knapik 6 AUG 04
Chairman, IACUC Date

DISTR: Study File, QAU, Archives, Sponsor

TOXICOLOGY PROGRAM
PROTOCOL MODIFICATION

Date of Modification: 10/25/04

Protocol Title: Subchronic Oral Toxicity of RDX in Rats

Study Director: Dr. Michael Major

MODIFICATION

Pg. para. section

1, Form 28E (8/5/04) Modification: The original modification stated that 281 animals would be required to repeat the entire study. This number will be lowered to 254.

Reason: After reviewing the results of the 14-day study, it was decided that 1 dose group could be dropped from the 90-day study. In addition, the number of health monitoring/extra animals was lowered from 21 to 14.

2, _____ Modification:

Reason:

3, _____ Modification:

Reason:

4, _____ Modification:

Reason:

Michael A Major 8 NOV 04
Study Director Date

25 Oct 04
Principal Investigator Date

NA
Chairman, AUC Date

DISTR: Study File, QAU, Archives, Sponsor

CHPPM Form 28-E, 1 May 1996 (MCHB-DL-TE)

MCHB-TS-TTE 7 October 2004

MEMORANDUM FOR RECORD

SUBJECT: Analytical Chemistry Support for DTOX Protocol # 5131-38-02-12-01, Subchronic Oral Toxicity of RDX in Rats.

During the Quality Assurance Inspection for the second phase of this study, it was discovered that no signature was obtained in the Analytical Chemistry Support space on the animal use protocol cover page. The request for chemistry support was submitted through SAMPNEWS and accepted by the DLS Explosives Chemistry Team, however, the appropriate DLS Program Manager signature needs to be obtained showing his approval for support of the second phase of the study. Therefore, this memorandum will show his approval for future support of this protocol and will be filed with the original protocol.

DTOX Principal Investigator — Date: 7 Oct 04

DLS Program Manager — Date: 13 Oct 2004

MCHB-TS-TTE October 12 2004

MEMORANDUM FOR RECORD

SUBJECT: Change in Attending Veterinarian for DTOX Protocol # 5131-38-02-12-01, Subchronic Oral Toxicity of RDX in Rats.

Due to complications occurring during the first subchronic rat study with RDX, the study must be repeated in order to obtain accurate results. A modification was submitted to the original protocol and approved by the IACUC in order to repeat the study under the same protocol number. For this reason, the protocol has been active since December of 2002. During this time, DTOX has had three attending veterinarians that will have worked on the study. The Strategic Initiatives Office has requested that this be documented in the form of a memorandum to be filed with the original protocol. MAJ Susan Goodwin was the DTOX attending veterinarian from the beginning of the study until June of 2003. MAJ Steven Dalel was the attending veterinarian from June of 2003 until August of 2004. MAJ Schiavetta has been the DTOX attending veterinarian since August of 2004 and will continue to be through the end of this study.

DTOX Principal Investigator — Date: 12 Oct 04

DTOX Attending Veterinarian — Date: 17 Oct 04